



# Odontogenic sinusitis: A state-of-the-art review

John R. Craig 

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, Michigan, USA

## Correspondence

John R. Craig, Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, 2799W Grand Blvd, Detroit, MI 48202, USA.  
Email: [jcraig1@hfhs.org](mailto:jcraig1@hfhs.org)

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## Abstract

Odontogenic sinusitis (ODS) is more common than historically reported, and is under-represented in the sinusitis literature. ODS is distinct from rhinosinusitis in that it is infectious sinusitis from an infectious dental source or a complication from dental procedures, and most commonly presents unilaterally. ODS clinical features, microbiology, and diagnostic and treatment paradigms are also distinct from rhinosinusitis. ODS evaluation and management should generally be conducted by both otolaryngologists and dental providers, and clinicians must be able to suspect and confirm the condition. ODS suspicion is driven by certain clinical features like unilateral maxillary sinus opacification on computed tomography, overt maxillary dental pathology on computed tomography, unilateral middle meatal purulence on nasal endoscopy, foul smell, and odontogenic bacteria in sinus cultures. Otolaryngologists should confirm the sinusitis through nasal endoscopy by assessing for middle meatal purulence, edema, or polyps. Dental providers should confirm dental pathology through appropriate examinations and imaging. Once ODS is confirmed, a multidisciplinary shared decision-making process should ensue to discuss risks and benefits of the timing and different types of dental and sinus surgical interventions. Oral antibiotics are generally ineffective at resolving ODS, especially when there is treatable dental pathology. When both the dental pathology and sinusitis are addressed, resolution can be expected in 90%–100% of cases. For treatable dental pathology, while primary dental treatment may resolve the sinusitis, a significant percentage of patients still require endoscopic sinus surgery. For patients with significant sinusitis symptom burdens, primary endoscopic sinus surgery is an option to resolve symptoms faster, followed by appropriate dental management. More well-designed studies are necessary across all areas of ODS.

## KEYWORDS

apical periodontitis, chronic rhinosinusitis, endoscopic sinus surgery, maxillary sinusitis, odontogenic sinusitis

## Highlights

- Odontogenic sinusitis (ODS) is one of the most common cause of unilateral maxillary sinus disease, but has been underrepresented in previous sinusitis literature.

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- Clinicians must be able to suspect ODS based on certain clinical features like unilateral middle meatal purulence on nasal endoscopy, subjective foul smell, and sinus computed tomography demonstrating maxillary sinus opacification with or without overt adjacent dental pathology.
- Diagnosing ODS requires confirmation of infectious sinusitis by otolaryngologists ideally with nasal endoscopy, and confirmation of adjacent maxillary dental pathology by dental specialists.
- Management centers on multidisciplinary collaboration and shared-decision making between otolaryngologists, dental specialists, and patients.

## INTRODUCTION

Odontogenic sinusitis (ODS) is a fascinating form of sinus disease that is truly distinct from other types of rhinosinusitis. ODS refers to bacterial maxillary sinusitis, with or without extension to other paranasal sinuses, secondary to either adjacent infectious maxillary dental pathology, or iatrogenic injury from dental procedures.<sup>1-3</sup> ODS may account for 25%–40% of all chronic maxillary sinusitis,<sup>4,5</sup> occurs unilaterally most commonly,<sup>6-14</sup> and represents 45%–75% of unilateral maxillary sinus opacification on computed tomography (CT).<sup>6-8,15</sup> ODS most commonly presents in the 5th decade of life, affects males and females equally, and patients typically have chronic symptoms (median, 6 months).<sup>2</sup> While ODS most commonly presents chronically, it can present acutely with extrasinus orbital, intracranial, or osseous infectious spread.<sup>16</sup> Potential dental pathologies causing ODS include apical periodontitis (AP; endodontic disease stemming from pulpal necrosis), marginal periodontitis, oroantral communication or fistula (OAC or OAF), or dental-treatment-related foreign bodies within the maxillary sinus.<sup>7,12,17-22</sup> AP and OAC/OAF have been the most commonly reported causes of ODS.<sup>2,22</sup>

Despite ODS being relatively common, it has flown under the literary radar. ODS has only represented about 1% of the sinusitis literature over the last 20 years.<sup>23</sup> In addition to low ODS publication volume, 90%–100% of published studies per decade over the last 30 years have been level 4–5 evidence.<sup>23,24</sup> Low publication volume and quality have likely contributed to ODS being underrepresented in even recent national and international sinusitis guidelines.<sup>25,26</sup> Additionally, these recent guidelines have not discussed how to diagnose or manage ODS. However, there has been an increase in ODS original research in the last decade with improved evidence levels for both ODS diagnosis and management. In just the last year, national and international consensus statements based on systematic literature reviews and expert panels have also been published with recommendations for diagnosing and treating ODS.<sup>1,3</sup>

This literature review will provide the most up-to-date evidence guiding current recommendations on diagnosing and managing ODS. Important clinical scenarios will also be discussed to highlight how these diagnostic and therapeutic recommendations can be implemented.

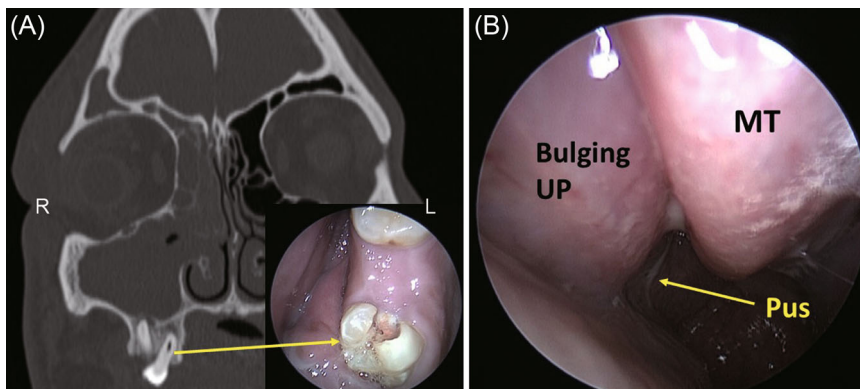
## DIAGNOSING ODS

While diagnosing ODS may seem intuitive by confirming sinusitis and an adjacent infectious dental source, it is not so straightforward based on prior literature. A recent systematic review of 63 ODS studies demonstrated high variability in the use of diagnostic criteria, and only 14 studies required multidisciplinary evaluations.<sup>27</sup> A recent international multidisciplinary consensus statement outlined a system for diagnosing ODS based on multidisciplinary evaluations by both otolaryngologists and dental specialists. The consensus was reached that diagnosing ODS requires two critical components: suspecting and confirming ODS. First, both otolaryngologists and dental providers must be able to suspect ODS based on certain clinical features, so that patients are then appropriately referred to the other provider necessary to confirm either the dental pathology or sinusitis. Second, otolaryngologists should confirm the infectious sinusitis through nasal endoscopy, and dental specialists should confirm the adjacent odontogenic pathology through specific examinations and imaging. Based on the diagnostic consensus, Figure 1 shows some of the key clinical features that should drive ODS suspicion, and the modalities by which sinusitis and different dental pathologies should be confirmed. A key point to highlight is that diagnosing ODS generally requires both dental providers and otolaryngologists. If one does not suspect ODS, it can easily be overlooked if the clinician only assesses for pathology specific to his or her specialty. Figure 2 shows a classic example of ODS due to AP, with confirmation of both infectious sinusitis endoscopically, and ipsilateral maxillary molar AP.

The diagnostic consensus statement outlined a number of clinical features that should arouse ODS suspicion based on original research and expert consensus. For example, subjective foul smell has been shown in two prospective cohort studies to be more specific for ODS.<sup>28,29</sup> ODS patients are also more likely to have purulence seen on nasal endoscopy compared to chronic rhinosinusitis.<sup>30,31</sup> With regard to sinus cultures, ODS patients have higher rates of alpha-hemolytic streptococcal species and anaerobes compared to rhinosinusitis patients.<sup>12,21,30,31</sup> Lastly, compared to rhinosinusitis, ODS tends to demonstrate relative sparing of the posterior ethmoid and sphenoid sinuses on CT.<sup>1,2,16,29</sup> All these clinical features reached consensus as being more associated with ODS compared to other forms of rhinosinusitis.

Suspect ODS	Confirm Sinusitis	Confirm Dental Pathology
<ul style="list-style-type: none"> <li>• Unilateral sinusitis symptoms</li> <li>• Foul smell</li> <li>• Unilateral maxillary sinus opacification on CT</li> <li>• Possible dental pathology on CT</li> <li>• Unilateral middle meatal purulence on nasal endoscopy</li> <li>• Odontogenic bacteria in sinus culture</li> </ul>	<ul style="list-style-type: none"> <li>• Nasal endoscopy: purulence, edema, polyps</li> <li>• Tentative confirmation: negative or inconclusive endoscopy, but ODS suspicion based on clinical features</li> </ul>	<ul style="list-style-type: none"> <li>• Endodontic (AP): cold pulp test, periapical imaging (CBCT, PAR, OP)</li> <li>• OAF: oral examination (patients blow nose against occluded nares, or probing of the fistula)</li> <li>• Dental implants: assess for peri-implantitis or implant instability (mobile)</li> </ul>

**FIGURE 1** Diagram highlighting the two central tenets of diagnosing odontogenic sinusitis (ODS): suspecting and confirming the condition (as described in international multidisciplinary consensus).<sup>1</sup> The diagnosis of ODS is made by confirming sinusitis through nasal endoscopy by otolaryngologists and confirming adjacent maxillary dental pathology through various forms of diagnostic testing and imaging by dental specialists. AP, apical periodontitis; CBCT, cone beam computed tomography; CT, computed tomography; OAF, oroantral fistula; OP, orthopantomogram; PAR, periapical X-ray



**FIGURE 2** (A) Computed tomography demonstrating right-sided odontogenic sinusitis due to apical periodontitis that arose from dental caries and pulpal necrosis in a maxillary molar (yellow arrow pointing to the carious molar). (B) Right-sided nasal endoscopy demonstrating an edematous bulging uncinat process (UP), with purulence draining posteriorly in the middle meatus. MT, middle turbinate

There are some other important nuances to appreciate when evaluating ODS as well. First, clinicians cannot rely on radiologists to detect ODS, as multiple studies have shown that they miss the dental pathology on CT in 60%–70% of cases.<sup>6,10,11</sup> Second, patients often have no dental pain,<sup>1,2,10,32</sup> and rarely divulge their dental history.<sup>7</sup> Lastly, some cases of ODS due to endodontic disease have no overt dental pathology on CT.<sup>10,29</sup> Each of these issues reinforces how important it is for clinicians to be able to suspect ODS based on the clinical features outlined in Figure 1.

## MANAGING ODS

One overarching theme with ODS management is that when both the dental pathology and sinusitis are addressed, the condition should resolve in 90%–100% of cases.<sup>3</sup> However, optimal ODS

management depends on the type of dental pathology, patients' symptom burdens, and whether there are extrasinus infectious complications.

For ODS, one must first consider whether patients have any treatable dental pathology. Treatable dental pathologies causing ODS include OAF, ODS after maxillary sinus bone grafting or dental implants, and AP with or without periapical lesions. While marginal periodontitis has been reported as a cause of ODS, very little has been published on this condition, and no studies have reported on its treatment in the setting of ODS. In some ODS cases, there is no treatable dental pathology, such as in ODS after dental procedures that cause a temporary OAC, surgically closed OAF, or maxillary sinus dental foreign bodies with no OAF. In these cases, no dental intervention is necessary, and surgeons must consider medical therapy versus transnasal endoscopic or transoral approaches to remove any foreign body and ventilate the sinus.

## Medical management

As ODS represents bacterial sinusitis, it would seem reasonable to prescribe oral antibiotics initially. However, for ODS due to treatable dental pathology, multiple case series or cohort studies have demonstrated poor oral antibiotic efficacy. Therefore, a multi-disciplinary consensus was reached that antibiotics are not curative for ODS due to treatable dental pathology, and should generally be considered a temporizing measure.<sup>3</sup> No study has specifically studied the utility of antibiotics in cases of ODS without treatable dental pathology, but in case series that have included such patients, antibiotics have still generally been unsuccessful. Future studies are necessary to determine the utility of antibiotics for different types of ODS.

No studies have analyzed whether ODS patients benefit from other adjunctive treatments described for rhinosinusitis patients like topical saline irrigations, or topical or oral decongestants.<sup>33</sup> Future studies would be necessary to determine the utility of such adjunctive therapies in ODS.

## Surgical management

For ODS due to OAF, multiple studies have demonstrated 90%–100% success when both ESS and OAF closure are performed either concurrently or in close proximity,<sup>13,34–36</sup> but no studies to date have compared OAF closure alone to endoscopic sinus surgery (ESS) plus OAF closure. Future studies are needed to determine whether ESS improves the success of OAF closure for ODS due to OAF and whether ESS timing affects success.

For dental implant-related ODS, there has been a preponderance of success with primary ESS rather than dental implant removal, although only from small case series.<sup>3</sup> Dental implant removal is not necessary unless there is peri-implantitis or the implant is mobile.<sup>37,38</sup> Implant removal may be associated with an increased risk of OAF development, more challenging reimplantation, and significant patient costs.<sup>37</sup> A multidisciplinary approach should be taken with these cases, with evaluations by both otolaryngologists and dental specialists.

One of the more controversial management paradigms is for ODS due to AP. Primary dental treatment options are root canal therapy (RCTx) or dental extraction. While both have been reportedly used to treat ODS, more evidence on success rates exists for dental extraction. While RCTx has been used successfully for ODS, it has only been reported in case reports,<sup>39,40</sup> or small series,<sup>14,41,42</sup> and success rates cannot be determined. The average published success rate for primary dental extraction for ODS due to AP is about 60%.<sup>32,42–45</sup> However, this success rate should be viewed with caution for multiple reasons. First, most of these studies have had small sample sizes and have represented level 4 evidence. Second, some of the studies have utilized both RCTx in addition to extraction, without specifying frequencies of each intervention. Third, studies recently have often not reported sinus disease extent on CT, and

some have included patients with isolated maxillary sinus mucosal thickening, which may not represent infectious ODS. Studies have also been heterogeneous with regard to antibiotic use before and after dental treatment. Lastly, studies have largely not reported time to sinusitis resolution, and have demonstrated wide variability in follow-up durations and in methods of measuring sinusitis resolution.

Two recent prospective studies have demonstrated higher success rates for dental extraction at resolving ODS due to AP compared to previous studies. Yoo et al.<sup>44</sup> followed 33 patients prospectively and reported a 67% success rate (27 extractions, 4 RCTx). They reported that preoperative smoking and higher Lund–Mackay scores portended a worse prognosis for dental treatment. Simuntis et al.<sup>43</sup> published the largest prospective series to date on 96 patients with ODS due to AP. They demonstrated a 77% success rate with dental extraction alone, with the remainder requiring subsequent ESS. They showed that persistent foul smell 2 weeks after extraction was associated with extraction failure. However, some important study limitations should be discussed. First, they included patients with isolated maxillary sinus disease with varying degrees of mucosal thickening but did not report pretreatment nasal endoscopy. Therefore, some of their included patients may not have had infectious sinusitis. Additionally, patients who had true ODS had more limited disease than has been reported in the literature, since 70% of published ODS cases have had at least ethmoid disease, and 40% frontal disease.<sup>2</sup> It has been shown that more severe sinusitis extent based on higher Lund–Mackay scores leads to lower primary dental treatment success,<sup>32,44</sup> so the higher success rate demonstrated by Simuntis et al.<sup>43</sup> could be explained partly by their patients' lower sinusitis disease burdens.

More well-designed studies are needed to determine the efficacies of primary RCTx and extraction at resolving ODS due to AP. Importantly, studies should include multidisciplinary evaluations by otolaryngologists and dental providers, include only ODS patients with sinus opacification (not isolated mucosal thickening), stratify patients by maxillary versus extramaxillary sinus involvement, and analyze time to sinusitis resolution.

Another controversial aspect of ODS management is the timing of primary ESS versus dental treatment. When ODS is due to treatable dental infectious pathology, it is intuitive to treat the tooth first, then reserve ESS for dental treatment failures. While multiple prior ODS case series and review articles have reported that primary dental treatment is critical to ODS management, published data show primary dental treatment being successful in only about 50%–60% of cases, and have rarely reported time to sinusitis resolution. Craig et al. showed in a prospective cohort study of 37 patients that patients who underwent primary ESS had significantly faster resolution of sinusitis symptoms and endoscopy findings by 7–12 days, compared to 35–56 days for primary RCTx or extraction patients.<sup>14</sup> Further supporting these recommendations, Choi et al. recently showed no difference in outcomes between patients who underwent primary or secondary ESS, as long as both the dental and sinus disease were addressed.<sup>46</sup> Additionally, a multidisciplinary consensus panel recently concluded that in ODS patients with significant

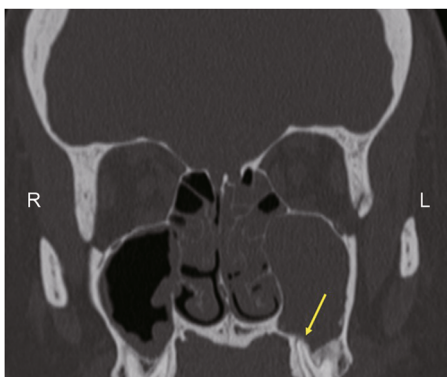
sinusitis burdens, primary ESS should be considered to control symptoms, followed by appropriate dental treatment.<sup>3</sup>

A final interesting point relates to sinus surgery extent in ODS patients undergoing ESS. While most studies to date have described opening all diseased sinuses based on preoperative imaging,<sup>13,14,35,37,38</sup> two prospective series from a single institution have demonstrated success with maxillary antrostomy alone in uncomplicated ODS patients even with frontal sinus involvement.<sup>47,48</sup> Additionally, the recent ODS management consensus statement did not reach consensus on one item pertaining to ESS extent for uncomplicated ODS. For uncomplicated ODS (i.e., no extrasinus spread), it was agreed that maxillary antrostomy alone is an option, regardless of sinusitis extent, but opening all diseased sinuses is also reasonable. More research is needed to determine the optimal extent of surgery for uncomplicated ODS. For complicated ODS with extrasinus spread, a consensus was reached that all diseased sinuses should be opened.<sup>3</sup> Another important point in the consensus study was that balloon sinuplasty may not be appropriate for ODS due to frequent severe middle meatal and maxillary sinus edema or polyps, which could prevent adequate sinus ventilation and drainage of sinus purulence.<sup>3</sup>

In summary, until higher levels of evidence are achieved, ODS management centers on multidisciplinary shared decision-making between otolaryngologists, dental specialists, and patients, discussing the risks and benefits of different dental and sinus surgical treatment options, and the order in which treatments are performed.

## IMPORTANT CLINICAL SCENARIOS

1. Confirmed sinusitis and suspected ODS, but no overt dental pathology on CT scan (Figure 3). At least two studies have shown that approximately 30% of patients with ODS due to AP have

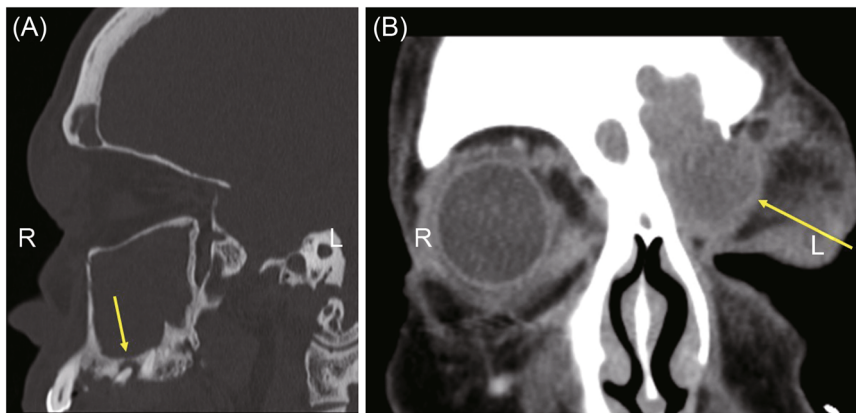
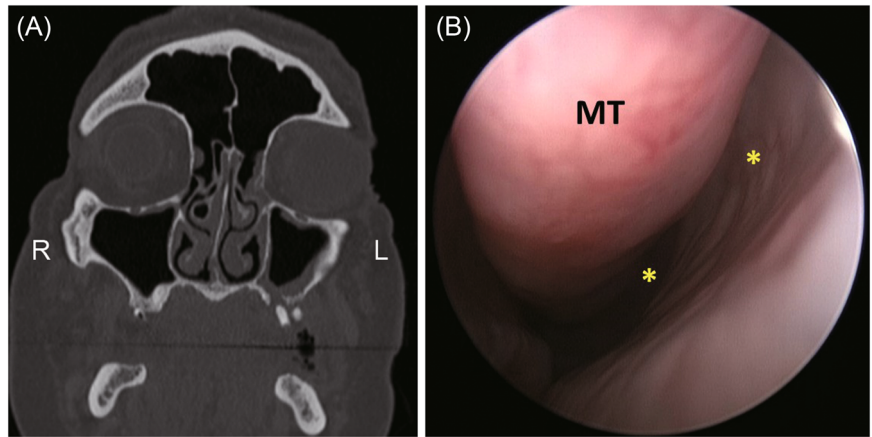


**FIGURE 3** Computed tomography demonstrating left-sided odontogenic sinusitis with maxillary and ethmoid sinus opacification, but no overt maxillary molar pathology. However, the periapical bone around the palatal molar root was remodeled or absent (yellow arrow). Due to an odontogenic sinusitis suspicion, the patient was referred to an endodontist who confirmed pulpal necrosis and apical periodontitis

very subtle to absent periapical pathology on CT scans.<sup>10,29</sup> While more studies are necessary, otolaryngologists should be aware that patients with unilateral maxillary sinus opacification can still have ODS even when no dental pathology is seen on CT. If these patients have other clinical features suspicious for ODS, they should still be referred to a dental specialist for at least endodontic testing and imaging.

2. Confirmed sinusitis and suspected ODS, but an inconclusive dental evaluation, with or without possible dental pathology seen on CT. There are some cases where dental pathology cannot be definitively confirmed, and patients may require intervention as a means of diagnostic confirmation. For example, some patients may have unilateral purulent sinusitis based on nasal endoscopy and clinical features suspicious for ODS, but dental evaluations may be inconclusive in the setting of intact asymptomatic dentition. In these situations, the patient may undergo ESS when medical therapy fails, but if sinusitis persists, patients should undergo repeat dental evaluations.<sup>1</sup> If evaluations continue to be inconclusive, some patients may require dental intervention as a means to both treat the sinusitis, and indirectly confirm the dental pathology based on response to treatment.
3. Confirmed dental pathology and suspected ODS, but inconclusive nasal endoscopy. In this scenario, if nasal endoscopy is negative or inconclusive due to an inadequate view of the middle meatus, the sinusitis could be tentatively confirmed based on suspicious clinical features outlined in Figure 1, such as subjective foul smell or a CT scan demonstrating maxillary sinus opacification. Ultimately, the infectious sinusitis could only be definitively confirmed through maxillary antrostomy and intraoperative assessment for maxillary sinus purulence.
4. Confirmed dental pathology, but only maxillary sinus mucosal thickening on CT (Figure 4). The recent consensus was reached that this is generally not ODS unless there is endoscopic evidence of purulence in the middle meatus or maxillary sinus.<sup>1</sup> This is important because maxillary sinus mucosal thickening is highly prevalent in 45%-100% of patients with maxillary dental pathology or prior dental work,<sup>49-52</sup> but this is generally not infectious sinusitis.<sup>2</sup> Unfortunately, some studies have considered patients with dental pathology and adjacent maxillary sinus mucosal thickening to represent ODS, and this could account for some discrepancies between studies with regard to diagnostic findings and treatment outcomes. Figure 4 shows a case of left-sided maxillary sinus mucosal thickening adjacent to a molar with confirmed AP. Since the nasal endoscopy was normal, this patient would not be diagnosed with ODS. In these situations, patients should have their dental pathology treated, and they can be followed thereafter for the development of infectious sinusitis. If dental providers suspect infectious sinusitis, they should refer patients to otolaryngologists for nasal endoscopy.<sup>1</sup>
5. Confirmed ODS due to dental pathology requiring extraction. In these situations, when considering the timing of extraction versus ESS, one must consider the likelihood of an OAC at the time of extraction followed by an OAF if the OAC does not close. Is this

**FIGURE 4** (A) Computed tomography illustrating a case of confirmed left maxillary molar endodontic and periodontal disease causing periapical bone erosion, and adjacent maxillary sinus mucosal thickening on computed tomography. However, the patient had a (B) normal left-sided nasal endoscopy with no purulence or edema in the middle meatus (yellow asterisks). Therefore this patient was not diagnosed with odontogenic sinusitis. MT, middle turbinate



**FIGURE 5** Example of odontogenic sinusitis causing an orbital subperiosteal abscess, resulting in left orbital pain and proptosis but no vision loss. (A) Sagittal noncontrast computed tomography demonstrating complete maxillary and frontal sinus opacification and a maxillary premolar root with a periapical lesion and bone erosion (yellow arrow). (B) Coronal computed tomography with contrast demonstrating left frontal sinus opacification and sinus floor erosion, and a superiorly based rim-enhancing subperiosteal orbital abscess (yellow arrow)

risk higher in the presence of infectious maxillary sinusitis? While some studies have demonstrated OACs to occur after maxillary molar dental extractions in only 0.5%–5% of cases,<sup>53</sup> studies have not reported the incidence of subsequent OAFs, or whether ODS increases the risk of OAC or OAF after dental extraction. One study showed that while OACs occurred in only 0.5%–1% of maxillary dental extractions posterior to canines, OAFs occurred most commonly in teeth with dentoalveolar abscesses (53% of all OAFs).<sup>54</sup> As dentoalveolar abscesses with periapical bone erosion are common in ODS, it is possible that OACs would be more common if extractions are performed in the setting of ODS, and purulence draining through the OAC could increase the risk of OAF. One could therefore argue that primary ESS could decrease the risk of OAC and OAF by clearing the maxillary sinus infection first, followed by dental extraction. Until more evidence is available to guide this decision, otolaryngologists and dental providers should discuss the risks and benefits of primary dental extraction versus ESS with patients on a case-by-case basis to determine the most optimal therapeutic approach.

- Asymptomatic ODS. Based on a recent multidisciplinary literature review, ODS can be asymptomatic in about 15% of cases with regard to dental and sinus symptoms (published range = 1%–47%). What should be done for these patients? While no studies have reported on the clinical course of asymptomatic ODS, a shared decision-making process should still ensue. One point to highlight to these patients is the potential for extrasinus infectious spread.<sup>16</sup> Therefore patients should be encouraged at a minimum to undergo dental treatment to eliminate the dental infectious source. Thereafter, patients should be monitored for resolution of the infectious sinusitis, ideally with nasal endoscopy. For persistent sinusitis, there should be a discussion of the risks and benefits of ESS to prevent future complications or to address sinusitis symptoms if they develop.
- Orbital, intracranial, and osseous complications from ODS (Figure 5). While uncommon overall, evidence on extrasinus spread of ODS has come largely from case reports. Complicated ODS has not been specifically discussed in recent sinusitis

guidelines,<sup>25,26</sup> but some recent studies have demonstrated that ODS should be considered in patients with complicated sinusitis. Nallani et al.<sup>55</sup> showed in a recent retrospective series of 17 frontal osteomyelitis cases that about 50% had dental pathology and sinusitis ipsilateral to both the dental and frontal disease on CT. Dental testing was not reported, but it is likely that some or all these patients had complicated ODS. Craig et al.<sup>2</sup> recently performed a systematic review of all complicated ODS publications, and 110 were identified. Based on this systematic review and a prior literature review, complicated ODS represents approximately 7% or less of all published ODS cases. Orbital complications represented 69% of complicated ODS, with intracranial and osseous complications representing 19% and 4% of cases, respectively. One potentially concerning finding was that of patients presenting with vision loss in the setting of ODS-related orbital complications, only 50% recovered vision. This was noted to be substantially worse than vision recovery rates reported in the complicated rhinosinusitis literature. Clinicians should assess for odontogenic sources in all cases of complicated sinusitis. Multidisciplinary management of complicated ODS is essential to drain extrasinus abscesses and to eliminate the infectious dental and sinus sources.<sup>16</sup>

## CONCLUSIONS

ODS is a common form of sinus disease and generally presents unilaterally. Both otolaryngologists and dental specialists should be able to suspect the condition and confirm both the infectious sinusitis and adjacent dental pathology. Multidisciplinary collaboration is generally essential to diagnose and treat ODS, so otolaryngologists and dental specialists should develop collaborative relationships in their regions to optimize the care of these patients. High success rates can be achieved when both dental treatment and ESS are performed, and the timing of treatments may depend on patients' symptom burdens. More well-designed studies are necessary to continue to make meaningful progress in diagnosing and managing ODS.

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## CONFLICT OF INTEREST

The author declares no conflict of interest.

## AUTHOR CONTRIBUTION

Dr. John R. Crag was the sole author of this manuscript.

## DATA AVAILABILITY STATEMENT

Data are available via source literature, for which all citations are included in the manuscript.

## ORCID

John R. Craig  <http://orcid.org/0000-0002-7377-4782>

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