ROAD MAP

➤ Definition.
➤ pathophysiology.
➤ Diagnosis.
➤ Grading systems.
➤ Clinical implications.
➤ Management.
OSTEITIS

Presence of new bone formation, fibrosis, inflammatory cells, periosteal thickening and a varying degree of increased osteoblastic–osteoclastic activity, as shown by the disruption of organized lamellar bone and formation of immature woven bone.

The exact process of how osteitis occurs is still not thoroughly understood.

Bacterial vs. inflammatory.

**Inflammatory mediators**

**Bone formation, fibrosis, inflammatory cell infiltration, periosteal thickening, increased osteoblastic–osteoclastic activity,**

**Disruption of organized lamellar bone and formation of immature woven bone.**

**PATHOPHYSIOLOGY**

*On a molecular level:*

➤ Bony remodeling on the cellular level is influenced by prostaglandins, leukotrienes, growth factors, and inflammatory cytokines.

➤ Osteoblast and osteoclast activity are actively regulated by members of the transforming growth factor (TGF)-β superfamily.
   - TGF-β overexpression, lead to increased bone matrix formation.
   - The bone morphogenetic protein (BMP) family of cytokines.

   (Upregulation of BMP8 and BMP9 in the sinonasal tissues have been observed in a mouse model of CRS).

   - interleukin (IL)-6, IL-1β and TNF-α gene expression were noted in the bone tissue.

   (nasal fibroblasts stimulated with IL-1β take on the role of osteoblasts, and this activity was inhibited by macrolide antibiotics).

➤ Matrix metalloproteinases (MMP9) up-regulated in CRS with osteitis.

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➤ Osteitis has been shown to be a migratory process with ability to spread via the bony Haversian canal system.

Studies demonstrated that, there is an initial widening of the Haversian canals within the bone and increased vascularity. This is associated with an inflammatory response within these vascular channels and later with fibrosis.

➤ Some authors have speculated that tissue remodeling changes become irreversible at some point, leading to the development of recalcitrant CRS.

DIAGNOSTIC METHOD

➤ There is no official gold standard diagnostic test for osteitis.
➤ Histology is considered the most accurate, and several grading systems have been proposed.
➤ Imaging:

   Less invasive methods have been developed to identify osteitis.
   - Computed tomography (CT).
   - Single photon emission CT (SPECT).

# Histopathological Grading System

<table>
<thead>
<tr>
<th>Study</th>
<th>Osteitis grade</th>
<th>Histopathological findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al. (2006)</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Minimal periosteal thickening</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Mild periosteal thickening with osteoblastic–osteoclastic activity</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Moderate periosteal thickening with wide osteoid seam and osteoblastic–osteoclastic activity</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Severe periosteal thickening and marrow formation</td>
</tr>
<tr>
<td>Biedlingmaier et al. (1996)</td>
<td>0</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Periosteal thickening</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Periosteal thickening, osteoblastic–osteoclastic activity, bone resorption and/or remodelling</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>Periosteal thickening, osteoblastic–osteoclastic activity, bone resorption and/or remodelling and wide osteoid seams</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Frank osteomyelitis, leucocytes and bone destruction</td>
</tr>
</tbody>
</table>

➤ Radiographic findings may differ depending on at what point in the disease process the CT is obtained.

➤ The possibility that the soft vs sclerotic appearance are distinct phenotypes of osteitis.

Soft bone formation may be an indication of rapid osteogenesis, whereas sclerotic bone may be a result of a more slow and organized process.

The presence of concurrent osteitis was assessed using both radiographic and pathological (bony remodeling) criteria.

diagnose osteitis based on thickness of bony partitions in the maxillary, ethmoid, and sphenoid sinuses

<table>
<thead>
<tr>
<th>Grade (per sinus)</th>
<th>Bony thickness (mm)</th>
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</thead>
<tbody>
<tr>
<td>Not significant</td>
<td>&lt;3</td>
</tr>
<tr>
<td>Mild</td>
<td>3</td>
</tr>
<tr>
<td>Moderate</td>
<td>4–5</td>
</tr>
<tr>
<td>Severe</td>
<td>&gt;5</td>
</tr>
</tbody>
</table>
RESULT

➤ The ethmoid sinus was the most frequently affected (82%), followed by the sphenoid (64%) and maxillary sinuses (45%).

➤ Both the radiographic and pathological incidence of osteitis were greater in patients with a history of prior surgery than those without.

➤ The extent of bony remodeling correlate with the severity of disease.

➤ More advanced bony changes associated with higher Lund-MacKay scores on CT.

**Kim et al Grading System (2006)**

- Proposed a system evaluating 3 separate reference points, with osteitis diagnosed when any single measurement exceeded 3 standard deviations above the reference range measured in a control group.

- No assessment of the frontal or the sphenoid sinuses.

<table>
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<th>Criteria measurement (mm)</th>
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<td>1. Maxillary sinus: posterolateral bony wall in the axial setting with the greatest dimension of maxillary sinus</td>
</tr>
<tr>
<td>2. Mean bony thickness of 3 randomly selected ethmoid septa</td>
</tr>
<tr>
<td>3. Midpoint of middle turbinate in the axial section showing the largest middle turbinate</td>
</tr>
</tbody>
</table>

**Diagnosis:** Any single measured value >3 standard deviations above reference range.

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Hyperostosis of the paranasal sinus might be a prognostic factor after primary ESS for CRS.

Radiological and pathological analysis.

Distinct method of CT analysis with the use of Hounsfield units (HU).

This unit represents an adjusted linear attenuation coefficient measurement where water is assigned a value of 0 and air is assigned a value of $-1000$.

Bone typically carries values between +400 and +1000 depending on density.

The HU proposed to be higher in the setting of new bone formation.

The authors categorized bone as hyperostotic when HU was greater than 500. The HUs were significantly increased with higher Lund-Mackay scores.

Global Osteitis Scoring Scale (2010)

- Each sinus given a grading ranging from 0 to 5.

- The grading per sinus was as follows:
  - Grade 1: Less than 50% of the sinus walls involved and osteitis <3 mm wide.
  - Grade 2: Less than 50% of the sinus was involved and 3–5 mm width.
  - Grade 3: Less than 50% of the sinus involved and wider than 5 mm or greater than 50% of the sinus wall involved and <3 mm wide osteitic changes.
  - Grade 4: Greater than 50% of the sinus wall involved and 3–5 mm.
  - Grade 5: Greater than 50% of the sinus wall and thicker than 5 mm.

- Global osteitis score (range: 0–50) osteitis classified as not significant (<5), mild (5–20), moderate (20–35) and severe (higher than 35).

Osteitis and Chronic Rhinosinusitis: LM Score

➤ Lund–Mackay scoring of mucosal disease correlated with Global Osteitis Scoring Scale.

➤ The majority of patients with osteitis had evidence of concurrent mucosal disease on the CT scan, and conversely, most patients with low Lund–Mackay (L–M) scores were free of significant osteitis.

A linear relation between the mean Global Osteitis Score and the number of previous surgeries, rising from 1.6 in patients with no previous surgeries to 3.6 to those who had undergone one sinus procedure to 15.5 to those with two previous operations to 31.5 in patients with more than six previous sinus surgeries.

Early studies correlated a diagnosis of CRS with a positive SPECT (higher score indicating more severe inflammation).

In a study comparing SPECT to CT for diagnosis of CRS, SPECT demonstrated an overall correlation of 57.9% (13.9% of sinuses positive on SPECT demonstrated no mucosal thickening on CT).

SPECT highly sensitive method for diagnosis of osteitis where acute or early bony involvement is detectable prior to visible thickening or increased density on CT.

In comparison to CT,

* SPECT has:
  - Additional cost, time to perform.
  - Radioactive exposure.
  - May not be useful as a stand-alone diagnostic study for an unspecified period of time following surgery due to bony remodeling.
  - Not useful for preoperative anatomic surgical planning.

Clinical Implications
Disease Severity, Symptom burden & Quality-of-Life Impact

<table>
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<tr>
<th>Study</th>
<th>Population</th>
<th>Marker of osteitis</th>
<th>Findings</th>
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<tr>
<td>Sacks et al. (2013)</td>
<td>n = 53</td>
<td>GOS and KOS scales</td>
<td>No correlation between presence or severity of osteitis at time of surgery and SNOT-22 and nasal symptom score at 12 months post-ESS</td>
</tr>
<tr>
<td>Snidvongs et al. (2012)</td>
<td>n = 88</td>
<td>GOS scale</td>
<td>No correlation between osteitis and disease severity as measured by SNOT-22</td>
</tr>
<tr>
<td>Bhandarkar et al. (2011)</td>
<td>n = 190</td>
<td>Bony thickening on CT</td>
<td>Osteitis correlated with worse baseline olfactory scores (SS), but no difference in baseline quality of life scores between patients with and without osteitis. Patients without osteitis more likely to exhibit clinically meaningful improvement on Rhinosinusitis Disability Index subscale scores after ESS (SS)</td>
</tr>
<tr>
<td>Georganas et al. (2010)</td>
<td>n = 102</td>
<td>GOS scale</td>
<td>Osteitis correlated with longer duration of symptoms (SS), but no correlation to symptom burden</td>
</tr>
<tr>
<td>Saylam et al. (2009)</td>
<td>n = 24</td>
<td>SPECT uptake</td>
<td>Poorer subjective response to medical treatment amongst those patients with osteitis</td>
</tr>
</tbody>
</table>

Surgical Outcomes

➤ A higher rate of recurrence of nasal polyps after endoscopic sinus surgery amongst those with osteitis.

In a recent study, it has been demonstrated that for those patients undergoing endoscopic modified Lothrop procedure, pre-operative severity of osteitis appears to be positively correlated with post surgical stenosis of the frontal neo-ostium.

➤ A few studies have resulted in conflicting findings.

Sacks et al. study, which found no association between the pre-operative presence or severity of osteitis and endoscopic severity scores 12 months after the operation.

# Researchs Summary

<table>
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<th>Study</th>
<th>Population</th>
<th>Marker of osteitis</th>
<th>Findings</th>
</tr>
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<tbody>
<tr>
<td>Zuo et al. (2014)</td>
<td>$n = 105$</td>
<td>KOS scale</td>
<td>Osteitis in ethmoid bone more severe in CRS patients without eosinophilia than those with eosinophilia (SS)</td>
</tr>
<tr>
<td>Ye et al. (2014)</td>
<td>$n = 25$</td>
<td>GOS scale</td>
<td>Pre-operative osteitis is a positive independent predictor of frontal neotuberculosis after Draf II procedure (SS)</td>
</tr>
<tr>
<td>Sacks et al. (2013)</td>
<td>$n = 53$</td>
<td>GOS and KOS scales</td>
<td>Osteitis associated with the need for a course of oral steroid post-ESS (SS), but no association found with number of infective exacerbations. No correlation between the presence or severity of osteitis at time of surgery and endoscopic severity scores at 12 months post-ESS</td>
</tr>
<tr>
<td>Snidvongs et al. (2012)</td>
<td>$n = 88$</td>
<td>GOS scale</td>
<td>Higher osteitis scores with increasing age. (SS). Osteitis correlated with the presence of polyps and previous surgery (SS). Osteitis correlated with greater disease severity score on endoscopy and CT (SS). Osteitis associated with greater serum and tissue eosinophilia (SS)</td>
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<td>Bhandarkar et al. (2011)</td>
<td>$n = 190$</td>
<td>Bony thickening on CT</td>
<td>Osteitis correlated with higher prevalence of nasal polyposis, previous surgery, and worse baseline CT and endoscopy scores (SS)</td>
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<td>Georgalas et al. (2010)</td>
<td>$n = 102$</td>
<td>GOS scale</td>
<td>Osteitis correlated with higher Lund–Mackay scores on CT and increasing number of previous operations (SS)</td>
</tr>
<tr>
<td>Telmesani et al. (2010)</td>
<td>$n = 82$</td>
<td>Histopathological changes</td>
<td>Greater proportion of patients with osteitis amongst those undergoing revision FESS (SS), and greater proportion of nasal polyps recurrence amongst those with osteitis</td>
</tr>
<tr>
<td>Saylam et al. (2009)</td>
<td>$n = 24$</td>
<td>SPECT uptake</td>
<td>Greater proportion of patients with osteitis amongst those with more extensive CRS disease as seen on CT</td>
</tr>
<tr>
<td>Cho et al. (2008)</td>
<td>$n = 65$</td>
<td>New bone formation and Hounsfeld units on CT</td>
<td>Osteitis worsens with ESS and is correlated with higher Lund–Mackay scores on CT (SS)</td>
</tr>
<tr>
<td>Cho et al. (2006)</td>
<td>$n = 23$</td>
<td>Hounsfeld units on CT</td>
<td>Osteitis correlated with higher Lund–Mackay scores on CT (SS)</td>
</tr>
<tr>
<td>Kim et al. (2006)</td>
<td>$n = 81$</td>
<td>Hyperostosis on CT</td>
<td>Osteitis correlated with poor postoperative outcome measured endoscopically (SS)</td>
</tr>
</tbody>
</table>

The management of osteitic bone in patients with CRS remains controversial.

➤ **Surgical:**
Removal/debridement of affected bone.

➤ **Medical:**
Prolong antibiotic use.

Will that change your practice?
In Conclusion ........