



# Osteitis and paranasal sinus inflammation: what we know and what we do not

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## **Purpose of review**

There is increased recognition of the high prevalence of osteitic changes affecting the bony framework of the sinuses in patients with chronic rhinosinusitis (CRS) with or without nasal polyps. However, their grading, clinical significance, and management remain controversial.

## **Recent findings**

A number of studies have confirmed that there is a clear correlation between radiological severity and extent of CRS, as measured with Lund-Mackay grading system and osteitis. However, there is little or no correlation between clinical severity and osteitis, with no evidence of worse quality of life or more nasal symptoms or headache in such patients. The number of previous surgeries appears to be closely correlated with the extent of sinusitis, although it is not clear whether that is a direct or a secondary association. Global Osteitis Grading Scale is a novel validated composite grading system – measuring the extent and severity of osteitis.

## **Summary**

Osteitis is more often present in patients with extended radiological disease and in patients undergoing revision surgery. More studies are necessary regarding its management, clinical implications, and natural course.

## **Keywords**

osteitis, rhinosinusitis, surgery

## **INTRODUCTION**

There is a subgroup of patients with chronic rhinosinusitis (CRS) whose symptoms persist despite maximal medical and surgical management. These patients with ‘difficult-to-treat rhinosinusitis’, as defined in the new European Position Paper on chronic rhinosinusitis and nasal polyps [1<sup>a</sup>], often exhibit areas of bony thickening and remodeling within their paranasal sinuses. Such areas have been alternatively described as osteitis, ostitis, or (neo)osteogenesis. In this review, we will present the current level of knowledge regarding osteitis in chronic rhinosinusitis with nasal polyps (CRSwNP) and chronic rhinosinusitis without nasal polyps (CRSsNP), with an emphasis on its clinical significance.

## **Definitions**

Terms that describe the inflammation of the sinonasal bony framework associated with radiologically visible abnormalities include ‘osteitis’, ‘osteomyelitis’, ‘hyperostosis’, ‘bone hyperplasia’, ‘bone remodelling’, and ‘neo-osteogenesis’. As there

is no marrow space in the flat bones around the sinus, we feel that the term osteomyelitis is not appropriate. Equally, although hyperostosis and neo-osteogenesis are often present, they are not always the main or even the predominant feature. In this review, we will be using the term osteitis in order to describe the bony changes associated with chronic inflammation in patients with CRSwNP and CRSsNP.

## **Histology: pathophysiology**

A number of animal studies [2–6] have demonstrated a link between experimentally induced rhinosinusitis and chronic inflammation of the bony middle turbinate as well as the ethmoid and maxillary sinus bony walls.

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### KEY POINTS

- The method of choice for the diagnosis of osteitis is the CT, in which osteitic bone appears as heterogeneous, irregular bone with areas of growth and destruction.
- A variety of grading scales has been described – the Global Osteitis Scoring Scale is a validated composite scale incorporating bony thickness, extent, and number of sinus involved.
- There is ample evidence that osteitis is associated with more extensive disease on CT and with previous surgery.
- There is no evidence that osteitis is linked with more debilitating symptoms or worse quality of life.
- There is some evidence that the presence of osteitis can be associated with worse outcome following surgery.

Four human studies focused on the pathological findings of bony inflammation in patients with CRS. Kennedy *et al.* [7] used radiolabeled tetracycline to assess bone remodeling of the ethmoid sinus and demonstrated higher bone activity with increased bone resorption and marked neo-osteogenesis in sinusitis patients compared with normal controls. Pathologically this corresponded to new bone formation, fibrosis, and the presence of inflammatory cells. Similar results were found by Giacchi *et al.* [8], who also assessed the bone of ethmoid sinus of CRS patients and compared it with control patients undergoing a CSF leak repair. He found periosteal thickening and increased osteoblastic–osteoclastic activity, disruption of organized lamellar bone, and formation of immature woven bone. Interestingly, the extent of bony remodeling was found to correlate with radiologically defined disease severity, with more advanced bony changes associated with higher Lund-Mackay (L-M) scores on computed tomography (CT). Histological samples of patients with rhinosinusitis were also analyzed by Lee *et al.* [9], who found pathological evidence of osteitis in 53% of their samples, ranging from 6.7% in those undergoing primary surgery increasing to 58% in patients having revision endoscopic sinus surgery (ESS). He also showed new bone formation in patients with CRS, with increased osteoid production and osteoblastic activity. Finally, Cho *et al.* [10] showed thickening of the periosteum and osteoblastic–osteoclastic activity in patients with CRS.

It is fair to say that what these studies demonstrated is that patients with chronic sinusitis tend to have bone formation, fibrosis, inflammatory cell infiltration, 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.

### Bacteriology

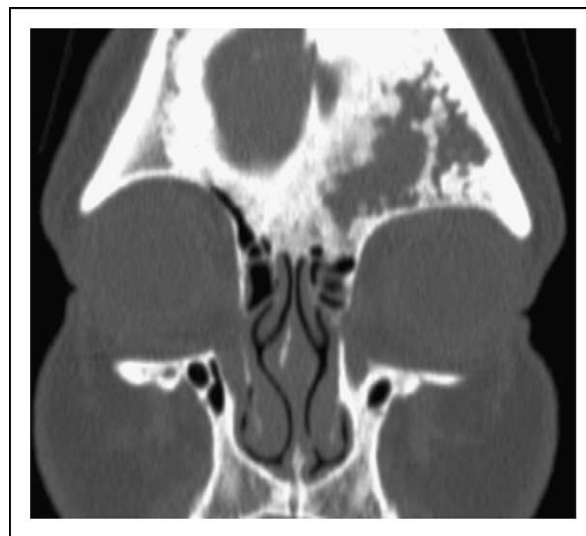
This chronic low-grade inflammation does not seem to be associated with direct bacterial invasion, as no group until now been able to demonstrate bacteria in the bone. Rather, it seems to both be stimulated by and act as a ‘depot’ of inflammatory cytokines [11,12], which ensure the persistence of disease, even when the mucosa is either treated medically or removed.

### Radiological features

Radiology is, in the vast majority of patients, the diagnostic modality of choice.

### Radiological features in computed tomography

In most studies, and certainly in current clinical practice, CT scan is the modality of choice in order to evaluate the presence and extent of osteitis in patients with CRS. Hence, osteitis is, almost always, a radiological diagnosis confirmed occasionally with pathological specimens taken during surgery. Radiological as well as clinical features can help, in most cases, to differentiate CRS osteitis from other bone diseases such as Paget’s disease or metabolic bone disease, as well as fibrous dysplasia (Fig. 1). In the case of patients with CRSwNP or CRSsNP, it is



**FIGURE 1.** Fibrous dysplasia in the left frontal sinus of a young male patient with no nasal symptoms and no history of previous sinus surgery.

important to record the presence and the extent of osteitic changes. To such effect, a composite grading system has been devised (Global Osteitis Scoring Scale – GOSS) that assesses bone thickness, the extent of involvement for each sinus, and the number of sinuses involved [13<sup>¶</sup>]. Osteitis is defined as loss of bone definition or hyperostosis or new bone formation or signal heterogeneity. The area of maximal thickness of each osteitic focus is measured (Fig. 2).

The scoring per sinus is as follows:

*Grade 1:* Less than 50% of the sinus walls involved and osteitis less than 3 mm wide.

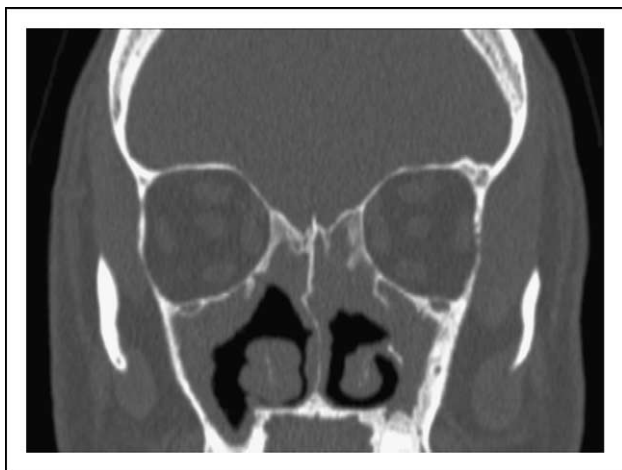
*Grade 2:* Less than 50% of the sinus was involved and 3–5 mm width.

*Grade 3:* Less than 50% of the sinus involved and wider than 5 mm or greater than 50% of the sinus wall involved and less than 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.

In this way, each sinus was given a grading ranging from 0 to 5. The scores of all 10 sinuses (right and left frontal, anterior ethmoid, posterior ethmoid, maxillary, and sphenoid) are added, producing a composite score (range 0–50). We have shown that the grading using this scale is easy to perform (usually 2–3 min per patient) and gives reproducible results. We found that inter-rater variability was low, and the agreement between different assessors, using intraclass correlation coefficient, was excellent (0.947). The best agreement was found for the maxillary sinuses and the lowest for the ethmoids. Using this grading scale, a direct



**FIGURE 2.** Evidence of Grade 3 osteitis of both ethmoid sinuses in a female patient who has undergone three previous sinus procedures for recalcitrant chronic rhinosinusitis.

correlation between L-M score and GOSS was found [13<sup>¶</sup>] (Fig. 3).

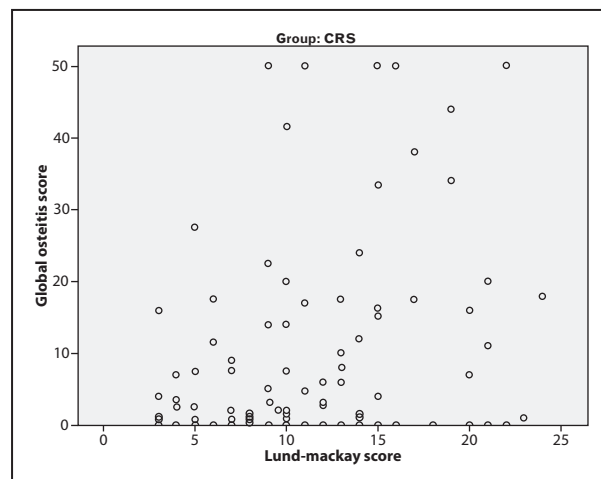
### Radiological features in single-photon emission computed tomography

Bone scintigraphy is considered the method of reference for the diagnosis of bone inflammation, although it is used rarely in everyday clinical practice. Two studies have assessed CRS patients with single-photon emission computed tomography (SPECT) scans. In the first study, 36 patients awaiting surgery for CRS underwent SPECT with technetium 99m-methylene diphosphonate. Thirty-two out of thirty-six were positive (increased uptake in the ethmoid sinus), and this result was confirmed with pathological findings in thirty-one (bone changes from lamellar to woven in the face of the bulla) [14].

Another study showed that 19 out of 24 patients with CRS had positive bone scintigraphy, with more positive results in patients with radiologically more extensive sinusitis [15].

### Incidence

Studies using CT, using various criteria to define osteitis showed that the incidence of radiological changes associated with bony inflammation in patients with CRS ranged between 4 [16], 36 [9], and 40% [13<sup>¶</sup>]. Both the study by Lee as well as the study by Richtsmeier found an increased incidence of osteitis in patients with higher L-M score, while another study found a greater incidence in patients undergoing revision surgery. Using the GOSS, we found that the incidence of osteitis was 33% in the nonoperated group compared to



**FIGURE 3.** Direct correlation between L-M scores and osteitis scores.

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75% in the operated group ( $P < 0.001$ ) [13<sup>■</sup>]. Interestingly, there was an almost 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, and to 31.5 in patients with more than 6 previous sinus surgeries ( $P < 0.001$ ) (Fig. 4).

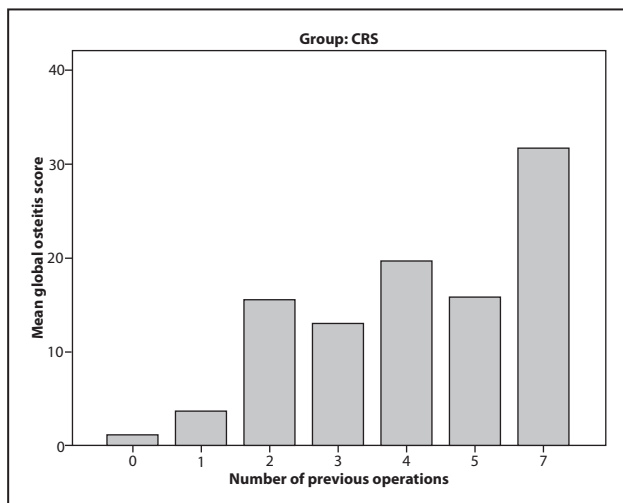
### Clinical implications

Although one would expect osteitis to be associated with more severe symptoms, this has not been shown: In our study [13<sup>■</sup>], there was no correlation between nasal rhino sinusitis outcome measure scores and the presence of osteitis. Specifically, using VAS to assess headache, there was no correlation between osteitis severity and headache [13<sup>■</sup>].

Similar results were found in a subsequent study from the USA, which used the Rhino-sinusitis Disability Index (RSDI) and chronic sinusitis survey (CSS) patients-reported outcome measures to assess patients with CRS and osteitis and failed to show any worse baseline quality-of-life (QOL) scores in patients with osteitis [17<sup>■</sup>].

### Radiological extent

Unlike subjective symptoms, radiological measures of disease extent seem to be worse in patients with osteitis. Both L-M scores as well as endoscopic scores have been shown to be correlated with osteitis in a number of studies [13<sup>■</sup>]. Many studies [9,13<sup>■</sup>,18] have confirmed the link between revision surgery



**FIGURE 4.** Number of previous surgeries is associated with the extent of osteitis.

and duration of symptoms with osteitis, although it remains unclear whether this is a primary or secondary association (underlying disease severity being the common factor).

### Prognostic factor

It appears that osteitis is an independent negative prognostic factor after ESS for CRS, both in terms of endoscopic grading of the outcome as well as in terms of QOL improvement after ESS [17<sup>■</sup>].

### Management

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

### Surgery

The idea of removing all involved bone, through drilling and the performance of radical procedures (Denker [19], Endoscopic modified Lothrop or Draf 3 [20]), is an attractive one. There is some evidence that an endonasal medical maxillectomy (Denker) may improve the outcome in patients with recalcitrant CRS [19]. However, its role – if any – in patients with osteitis is less well defined. Indeed, a recent study showed worse surgical outcomes in patients with osteitis [17<sup>■</sup>], while we should not forget that there is a direct correlation between the number of surgeries and osteitis [13<sup>■</sup>]. Although this could be a secondary association, both osteitis and number of surgeries being surrogate markers of severe disease, the possibility that surgery may trigger or exacerbate osteitis must also be kept in mind.

### Antibiotics (p.o. and i.v.)

The use of long-term antibiotics, especially macrolides, has been advocated in CRS, not only (or even primarily) for their antibacterial properties, but also in view of their direct anti-inflammatory action [21,22]. However, a recent large randomized multi-center trial has put doubts on it [23<sup>■</sup>], which is also reflected in the recent European Position Paper on rhinosinusitis guidelines [1<sup>■</sup>]. Unfortunately, the evidence of long-term antibiotics in osteitis is even more scarce: its advocates use the example of long bone osteomyelitis, to suggest that intravenous administration of antibiotics can produce high enough levels in the bone to clear an infection [24,25]. However, both studies suffer from methodological problems, number of participants, and lack of control group, while even more importantly, it is difficult to support such an intervention conceptually, when no group has yet demonstrated the presence of active, alive bacteria within areas of sinus osteitis.



## CONCLUSION

Osteitis is increasingly recognized as a common factor in cases of recalcitrant or difficult-to-treat rhinosinusitis. We do know that the number and extent of previous surgeries is associated with osteitis and that it is predictive of worse postoperative outcomes; however, the role if any of antibiotics or radical surgery in its management remains undefined.

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## Conflicts of interest

There are no conflicts of interest.

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- of special interest
- of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (pp. 000–000).

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