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The Histological Changes of Bones and Lining Mucosa in the Middle and Inferior Turbinate in Chronic Rhinosinusitis

Jahangir Ghorbani[1,2], Mitra Rezaei[2,3], Amir Sam Roshani Zaferanlo[4], Afsoon Zandi[1,2], Mahboobeh Karimi-Galougahi[1,2], Mahdi Khajavi[5,6]

1. Department of Otolaryngology, Masih Daneshvari Hospital, Shahid Beheshti University of Medical Sciences Tehran, Iran
2. Chronic Respiratory Disease Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran
3. Virology Research Center, National Research Institute of Tuberculosis and Lung diseases (NRITLD), Shahid Beheshti University of Medical Sciences, Tehran, Iran
4. Department of Otolaryngology-Head &Neck Surgery, Imam Khomeini University Hospital, Urmia, Iran.
5. Hearing Disorders Research Center, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
6. Department of Otorhinolaryngology, Loghman Hakim Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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Corresponding Authors:

Dr. Mahboobeh Karimi-Galougahi

Email:
mahboob76181@yahoo.com

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Abstract

Background: There is an association between osteitis and symptoms in chronic rhinosinusitis (CRS), but the exact clinical significance of osteitis is unclear. Most histological studies on osteitis of paranasal sinuses are limited to the ethmoid bone.

Aim: The current study examined the histologic changes of mucosa and bone in the middle turbinate and sphenoid sinus for comparison.

Methods: The current observational, cross-sectional study was conducted in a tertiary referral university hospital from September 2017 to September 2021. Consecutive adult patients with chronic rhinosinusitis symptoms who underwent endoscopic sinus surgery were enrolled in the study. Histopathological evaluations for the existence and level of inflammation were performed by a blinded pathologist regarding the history and imaging results. SPSS (version 26) was used to analyze the data and other analyses.

Results: Inflammatory changes of mucosa in the middle and inferior turbinates and sphenoid sinuses were more severe than inflammatory changes of bone in these areas (p values 0.006, 0.003, and 0.046, respectively).
There was no significant difference in the prevalence of bone and mucosal inflammation between the patients with polyps and those without polyps. We did not observe a significant difference in the prevalence of osteitis between the primary and revision surgery nor between patients with asthma and without asthma. There was an association between the severity of inflammatory changes of mucosa with bone in the middle and inferior turbinates and sphenoid sinus (p values 0.007, 0.002, and 0.037, respectively).

Conclusion: The present study indicates that chronic rhinosinusitis is not a disease that only involves mucosa. It is thus necessary to expand the boundaries of treatment beyond mere mucosa.

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Introduction

Osteitis is defined as bone inflammation without bone marrow involvement (1). Its histologic features in paranasal sinuses include osteogenesis and new woven bone formation (2). Nevertheless, the role of osteitis in sinusitis is unknown (3,4,5). Real osteitis with inflammatory infiltration of bone is not observed in histological evaluations of sinusitis; hence, it seems that osteitis is a misnomer (2). There are two different histologic and radiologic methods to detect osteitis in paranasal sinuses, and some studies have shown consistency between histologic and imaging criteria of osteitis of paranasal sinuses (5,6,7).

Classically, chronic sinusitis is associated with stomatal complex involvement; thus, the treatment is to find a way for drainage and ventilation, but it seems a new idea of inflammatory influx is more acceptable (8,9). Finding osteitis or inflammatory changes in bones in Sino nasal system in chronic rhinosinusitis may result in changes in the current understanding of its pathogenesis and treatment. Despite many studies considering the association of osteitis and symptoms in chronic rhino sinusitis (CRS), the exact clinical significance of osteitis is unclear (5,6,10). Most histological studies on osteitis of the paranasal sinus are limited to the ethmoid bone (11). The current study sought to determine the histological changes of bones in the middle and inferior turbinate and their lining mucosa in chronic rhinosinusitis. We examined the histologic changes of mucosa and bone in the middle turbinate and sphenoid sinus for comparison.

Methods

The study was conducted at a tertiary referral university hospital from September 2017 to September 2021. Adult patients (over 18 years old) with chronic rhinosinusitis symptoms who underwent endoscopic sinus surgery were enrolled in the study. The diagnosis of chronic rhinosinusitis was based on the European Position Paper on Rhinosinusitis and Nasal Polyps. Patients who did not respond to a 4-week course of systemic antibiotics and topical nasal steroid therapy were considered candidates for surgery. Patients with a history of immunodeficiency, cystic fibrosis (CF), mucociliary dysfunction, antrochoanal polyp, unilateral sinusitis, tumors, or those who received systemic corticosteroids within the previous month were excluded from the study.

The intranasal surgery was performed under general anesthesia and based on endoscopic sinus surgery standards. Samples of mucosa and bone were obtained from the inferior and middle nasal concha as well as the anterior wall of the sphenoid sinus. The specimens were fixed in formalin, and bone samples were decalcified in a solution of 10% formic acid and embedded in paraffin. Sections (4 μm) were stained with hematoxylin and eosin for light microscopy. A grading system for osteitis, suggested by Biedlingmaier and colleagues, was used, dividing bony changes into 5 grades. Similarly, a grading system consisting of 5 grades was used for mucosal inflammation. Histopathological evaluations for the presence and level of inflammation were performed by a pathologist who was blinded to the history and imaging results.

Data analysis was performed using SPSS version 26. All subjects signed an informed consent form before enrolling in the study, and the study protocol was approved by the Committee of Medical Ethics of Shahid Beheshti University of Medical Sciences.

Results

A total of 69 patients, with a mean age of 41.9 years (ranging from 22 to 74 years), took part in the study. Among the participants, 32 (46.4%) were male (refer to Table 1). Chronic rhinosinusitis with polyps (CRSwNP) was observed in 57 (82.6%) individuals, and 39 (56.5%) patients had asthma.

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A total of 64 middle and 61 inferior turbinates, as well as 62 sphenoid samples, were collected from the 69 subjects. Osteitis was found in 26 (40.6%) middle turbinates, 22 (36.1%) inferior turbinates, and 17 (27.4%) anterior wall sphenoid samples as per the histopathological examination.

The study also presented examples of different grades of inflammation in Figures 1-4. The majority of samples with osteitis were classified as grade 1, and no samples were classified as grade 3 or 4, meaning no clear evidence of osteomyelitis or inflammatory cell infiltration in the bone tissue was observed (refer to graphs 1-3).

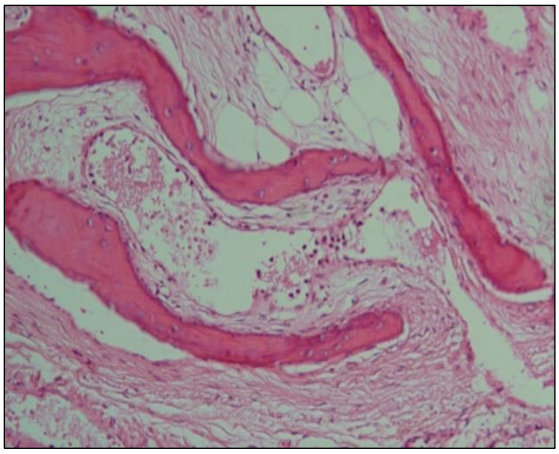

Figure 1. Grade 0 inflammatory bone involvement. Thin lamina propria with few vessels, thin trabeculae of mature lamellar bone, and a very thin periosteum were seen in histologic section.

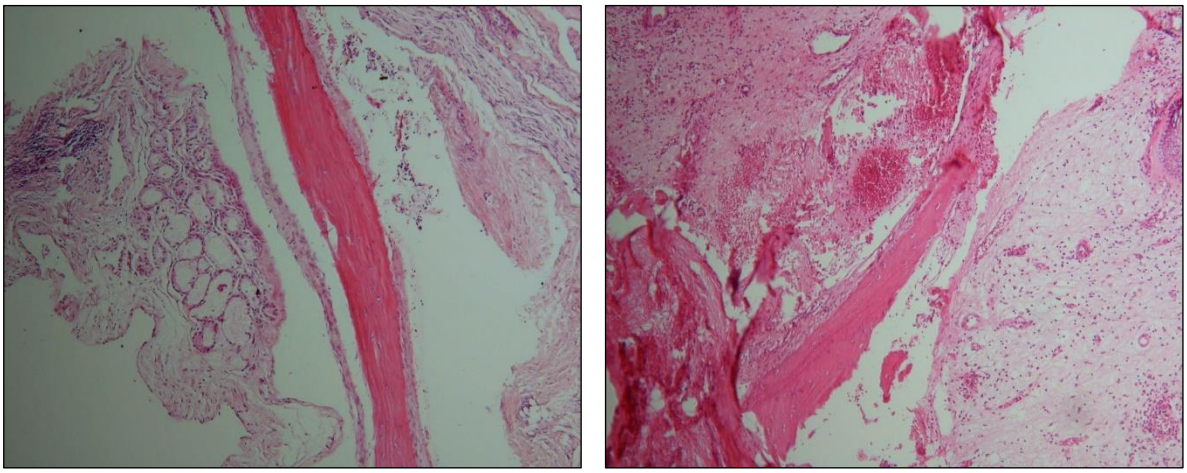

Figure 2. Left. Grade 1 bone, and Right, grade 2 mucosal inflammatory involvements. There are mild to moderate scattered chronic inflammatory cells infiltrate, with thick periosteum around the lamellar bone.

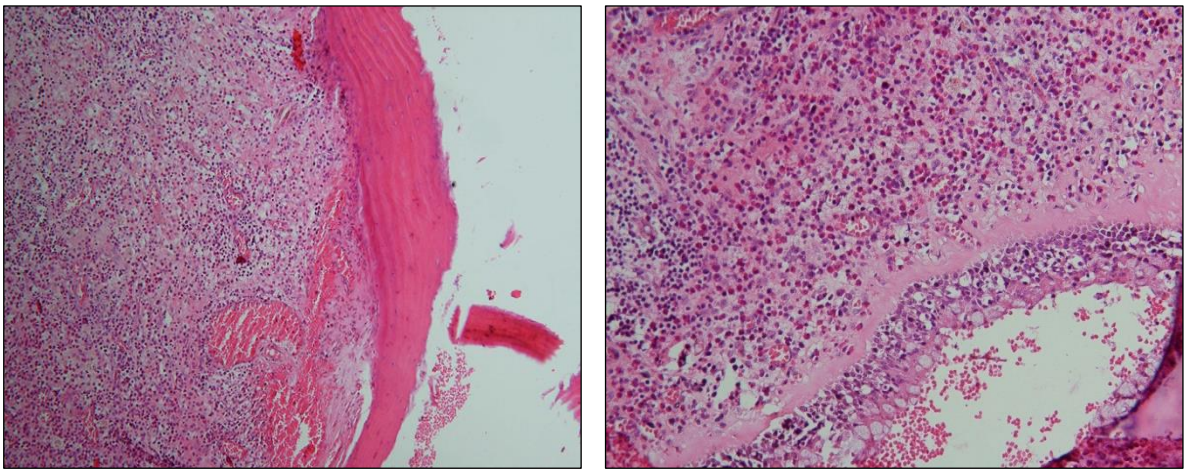

Figure 3. Left. Grade 2 bone and, Right, grade 3 mucosal inflammatory involvements. There are severe mixed inflammatory cells infiltrating the lamina propria, including numerous eosinophils, with thick periosteum around the lamellar bone in a histologic section..

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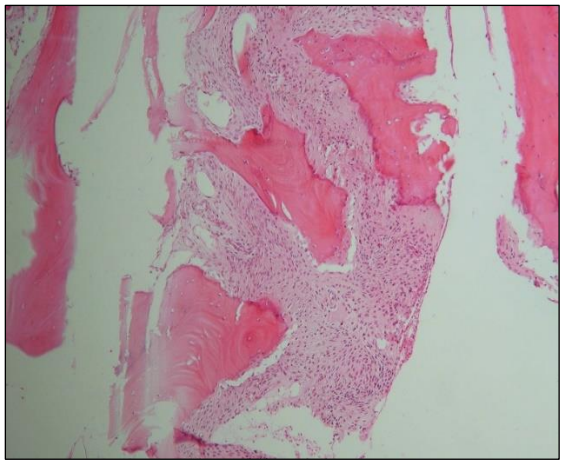
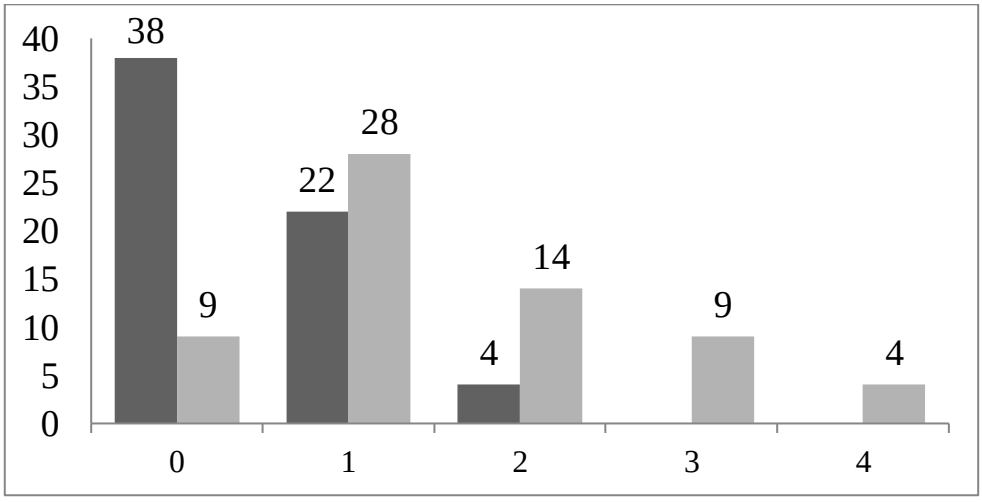
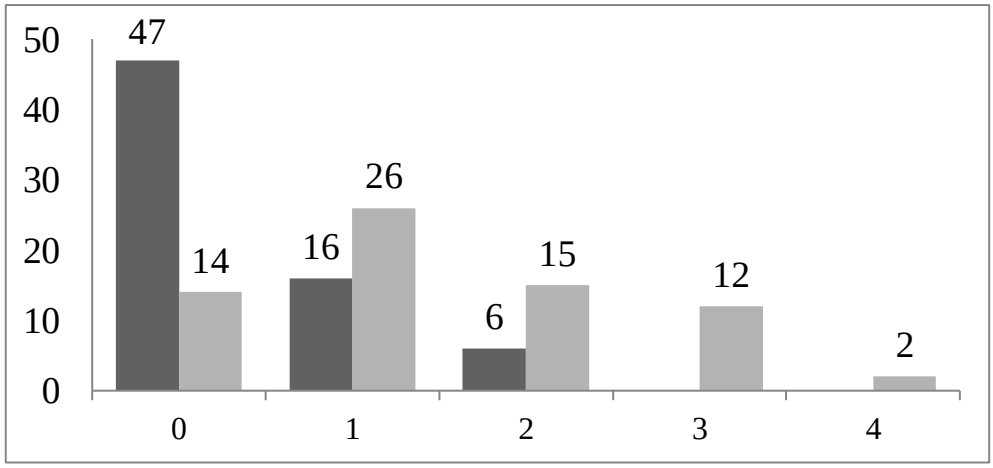


Figure 4. Grade 3 inflammatory bone involvement. Periosteal thickening, osteoblastic activity with bone resorption and remodeling in addition to wide osteoid matrix are seen in histologic section of bone.

Mucosal involvement was observed in 8 (86.6%) middle turbinates, 55 (80.9%) inferior turbinates, and 58 (85.3%) sphenoid samples (refer to graphs 1-3). Notably, mucosal involvement of the middle turbinate was not reported in 9 patients. The severity of mucosal inflammation ranged from grade 1 to grade 4 in the middle and inferior turbinates as well as the sphenoid. No significant differences were observed in the prevalence of bone and mucosal inflammation between patients with and without polyps. Similarly, no significant differences were found in the prevalence of osteitis between primary and revision surgeries, or between patients with and without asthma.



Graph 1. Distribution of different grades of inflammatory involvement of mucosa and bone of middle turbinate based on pathology, light and dark grey indicate mucosa and bone involvement, respectively.



Graph 2. Distribution of different grades of inflammatory involvement of mucosa and bone of inferior turbinate based on pathology, light, and dark grey indicates mucosa and bone involvement, respectively.

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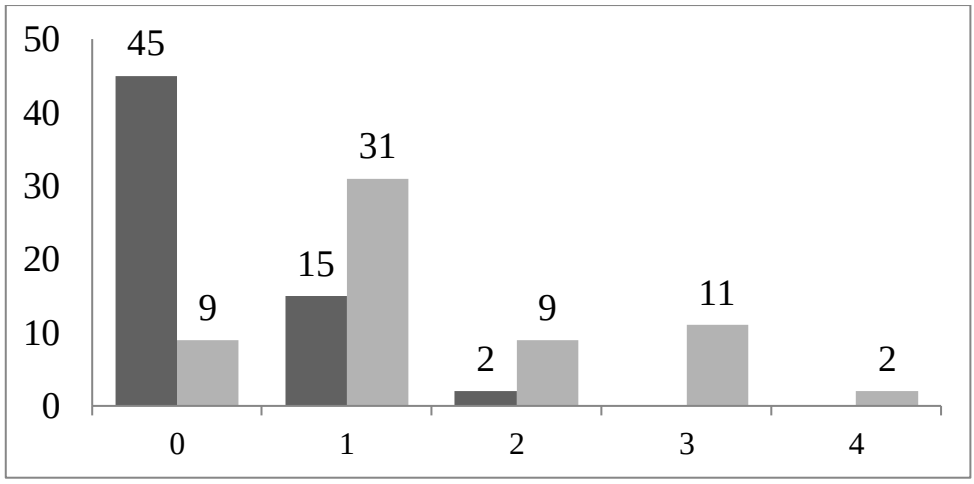

Graph 3. Distribution of different grades of inflammatory involvement of mucosa and bone of sphenoid sinus based on pathology, light, and dark grey indicates mucosa and bone involvement, respectively

In conclusion, the inflammatory changes of mucosa in the middle and inferior turbinates and sphenoid sinuses were more severe than the inflammatory changes of bone in these areas (p-values 0.006, 0.003, and 0.046, respectively). Additionally, an association was noted between the severity of inflammatory changes of the mucosa with bone in the middle and inferior turbinates as well as the sphenoid sinus (p-values 0.007, 0.002, and 0.037, respectively).

Discussion

It has been reported that osteitis may involve bones away from the sinus (15). The main goal of the current study was the evaluation of osteitis in additional sinus locations, including the middle and inferior turbinates in patients with chronic rhinosinusitis. To the best of our knowledge, this is the first study assessing osteitis on histopathological examination of the inferior turbinate in patients with chronic rhinosinusitis. Additionally, the present study investigated osteitis of middle and inferior turbinates and sphenoids; focusing on pathological findings that are more accurate than those of imaging examinations (14,16). We used histopathological methods for staging osteitis and mucosal involvement that provide the possibility to compare the severity of bone involvement to other similar studies. Osteitis in paranasal sinuses is usually studied based on histopathological or, in most cases, imaging examination. Most histopathological evaluations of chronic rhinosinusitis are focused on ethmoid sinus and particularly focus on mucosal changes (5). Only a few studies have examined histopathological changes in non-ethmoid bones (6,15,17,18,19,20). Although several studies on chronic rhinosinusitis reveal evidence of osteitis, no cause-effect relationship has yet been confirmed (5).

In the current study, the mucosa was histologically evaluated in terms of the existence and degree of inflammatory reactions, which showed mucosal involvement in the middle and inferior turbinates and sphenoid sinus in most (> 80%) cases. Only a few studies on the incidence of mucosal inflammation of inferior turbinate and sphenoid sinus mucosa are reported. Interestingly, the incidence of mucosal involvement of the ethmoid bone or middle turbinate was 100% in most studies (14,18,19), and only one study reported inflammatory infiltration of the inferior turbinate mucosa in chronic rhinosinusitis (21. No other study has reported the involvement of inferior turbinate mucosa.

There were no significant differences in the prevalence of bone and mucosal inflammatory changes between patients with chronic rhinosinusitis with and without nasal polyps,

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although the number of patients with chronic rhinosinusitis without nasal polyps was very low in the study. We also did not see a significant difference in the prevalence of osteitis between primary and revision surgery. In addition, no significant difference was observed between the number of patients with and without asthma. Consistent with our report, there was no association between osteitis and the presence of polyps, revision surgery, or asthma in a previous study (20). In contrast, another study showed a significant association between polyp and revision surgery with the presence of osteitis but they reported no association between asthma and osteitis (22,23).

The success of methods such as endoscopic mega-antrostomy and modified endoscopic medial maxillectomy to control chronic maxillary sinusitis, which usually is also associated with mucociliary clearance changes, may be partly due to the removal of osteitic bone of the inferior turbinate (24,25,26,27,28). The current study shows that osteitis of inferior turbinate may play a role in chronic maxillary sinusitis, particularly in treatment-resistant cases.

Osteitis in the middle turbinate may be an indication for considering resection of the middle turbinate at least in some cases. There were minor reported adverse effects after resection of the middle turbinate (14,29,30) and it is logical in the cases of severe or recurrent disease of frontal recess or anterior ethmoid area. Classically, a lateralized and scarified middle turbinate is a common reason for failed treatment in this area. Neo ostogenesis is a known cause of recurrent disease especially in frontal recess (31,32,33). Inflammatory involvement of bone and mucosa of the middle turbinate and the probability of extension of osteitis indicate the need for aggressive management of the middle turbinate to reduce inflammatory load (34). This may explain the high success rate of nasalization procedures that include complete resection of ethmoid lamellae, middle turbinate, and wide opening of sinuses (35).

Osteitis of the ethmoid, middle and inferior turbinate, and sphenoid sinus is shown in the current study indicating that the principle of ventilation and sinus drainage to treat sinusitis may not be adequate in all cases. In other words, mucosal treatment alone may not be adequate, and additional treatments for the involvement of bone may be necessary. Hence, the universal application of minimally invasive methods may be inadequate (25,36,37,38). While mucosal inflammation did not have any effect on the incidence of osteitis of ethmoid septa in one study (20), a correlation between the incidence of osteitis in ethmoid bone and the degree of mucosal pathology was shown in another study (19). In the present study, inflammatory involvement of mucosa was more common and more severe than inflammatory involvement of bone, nevertheless with a significant association between the severity of involvement in these two tissue types. Surgeons should therefore expect more severe involvement of bone in patients with more severe mucosal disease and consider more aggressive surgery.

Besides histological and physiological differences between middle and inferior turbinate (39,40), it seems that in both regions mucosa contributes to the inflammation of paranasal sinuses and we detected a correlation between these regions regarding inflammatory reactions. There is a simultaneous involvement of nasal and sinus mucosa in sinusitis; hence, rhinosinusitis is a more appropriate term for this disease. Although the prevalence of bone involvement in the inferior turbinate is lower in the middle turbinate, but higher than in the sphenoid sinus. Due to the considerable prevalence of mucosal and bone involvements of the inferior turbinate in pansinusitis, it seems that enough attention is not paid to the role of the inferior turbinate in chronic sinusitis. Further case-control investigations with larger sample sizes are warranted to clarify the

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involvement of the inferior turbinate in chronic sinusitis.

Our study has several limitations. Previous studies evaluating the mucosal inflammation in chronic rhinosinusitis have used different methods for staging inflammation, making direct comparison with our study difficult or impossible. This study was performed at a tertiary-level referral center in which most patients had asthma and nasal polyps, which may not represent the general population in the outpatient clinics. We did not investigate the role of individual markers and inflammatory cells like eosinophils in the bone histopathology of chronic rhinosinusitis. It is necessary to perform histopathologic studies in other Sino nasal bones in healthy individuals and patients with sinusitis to establish causality. Last, we did not examine the association between histological changes of mucosa and bone of Sino nasal system with clinical findings and their potential impact on treatment.

Conclusion

The present study indicates that chronic rhinosinusitis is not a disease that only involves mucosa. It is thus necessary to expand the boundaries of treatment beyond mere mucosa. In addition, confirming osteitis in locations other than ethmoid sinuses, such as inferior and middle nasal turbinate, may indicate the need for more aggressive surgery, specifically in cases with extensive or recurrent diseases.

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None to declare.

Conflicts of Interest

The authors declare no conflicts of interest.

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Ethical approval:

This study was ethically approved by the ethical committee of Shahid Beheshti University of Medical Sciences (date of approval: 2017/05/20) and project number 94127. Written informed consents were obtained from all included patients.

Author's contribution

Jahangir Ghorbani: concept, data collection and interpretation, writing. Mitra Rezaei: concept, data collection and interpretation, writing. Amir Sam Roshani Zaferanlo: concept, data interpretation, writing

Afsoon Zandi: concept, data interpretation, writing. Mahboobeh Karimi-Galougahi: concept, data collection and interpretation, writing.

Authors ORCIDs

Jahangir Ghorbani
https://orcid.org/0000-0001-6209-1081

Mitra Rezaei
https://orcid.org/0000-0002-7242-5839

Afsoon Zandi
https://orcid.org/0009-0003-4492-3034

Mahboobeh Karimi-Galougahi
https://orcid.org/0000-0001-9880-3802

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