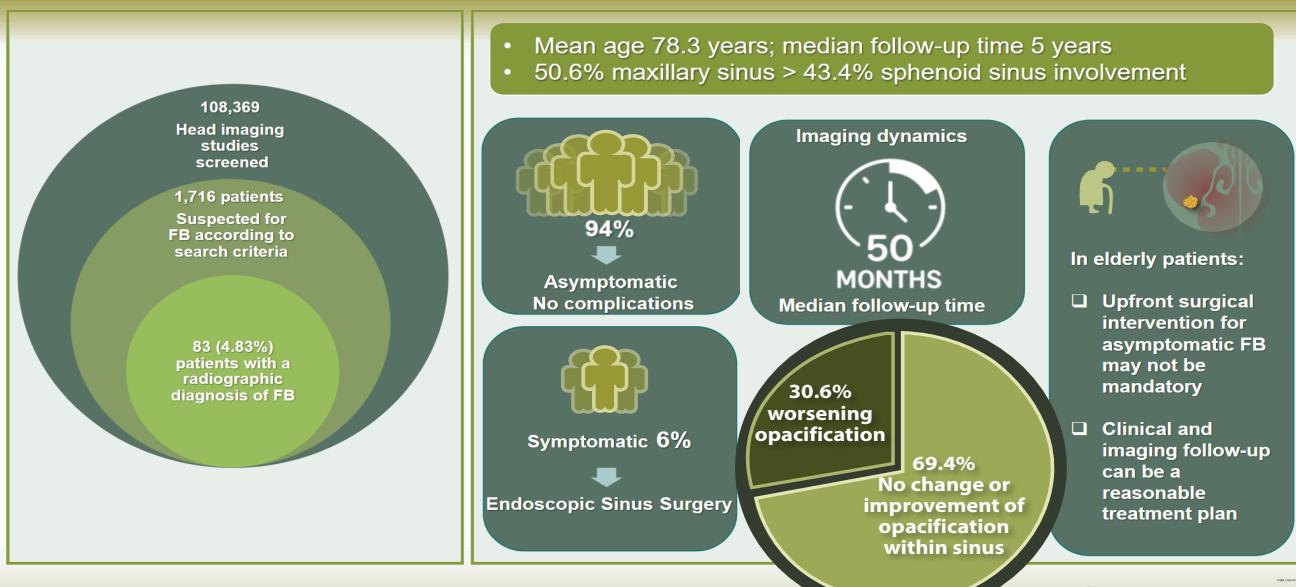


# Natural history of incidental paranasal sinus fungal balls: evidence from a decade-long imaging-based cohort

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## Natural history of incidental paranasal sinus Fungal Balls (FB)

Evidence from a decade-long imaging-based cohort



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## Abstract

**Introduction:** There is no data in the literature regarding the appropriate management of patients with an incidental finding of paranasal sinus fungal ball (FB) or its natural history. This study examined the long-term outcomes of a cohort of patients with FB, pooled from a large imaging database. **Methods:** A retrospective screening of 108,369 head imaging studies for phrases indicative of FB in a tertiary referral center, during 2012-2023. **Results:** A total of 1,716 patients were identified according to the search criteria and their imaging studies were evaluated by the authors. 83 (4.83%) patients were noted to have findings compatible with FB. Mean age was  $78.3 \pm 11.8$  years and median follow-up (FU) time was 59.2 (10.2-178.8) months. The most involved sinuses were maxillary (50.6%) and sphenoid (43.4%). Intra-sinus calcifications and sinus opacification were observed in all patients. Additionally, sinus wall bony sclerosis, and erosion were observed in 44.5% and 2.4%, respectively. 5 (6.0%) patients underwent surgery during follow-up. 4 (4.8%) patients had FB-associated symptoms, and 1 patient (1.2%) had posterior sphenoid sinus wall erosion. No morbidity or complications were reported for the remaining 78 (94%) patients who did not receive treatment. During a median interval of 50 months, 34/49 (69.4%) patients with  $\geq 2$  consecutive imaging studies showed no worsening of radiographic findings. **Conclusion:** During an average FU of 5 years of patients with incidental FB findings, the vast majority remained asymptomatic and without complications. Thus, upfront surgical intervention for asymptomatic FB in elderly fragile patients may not be mandatory and a clinical and imaging FU can be a reasonable treatment plan.

**Key words:** chronic sinusitis, health status, nasal surgical procedures, paranasal sinus disease, prevalence

## Introduction

Fungal ball (FB) sinusitis, previously referred to as mycetoma or aspergilloma, is a chronic and noninvasive mycotic disease<sup>(1)</sup>. Although asymptomatic fungal spores are frequently present in nasal cavities and typically do not require treatment, some patients may develop a fungal infection. *Aspergillus* is the most commonly identified pathogen that may develop into a FB in immunocompetent elderly patients<sup>(2)</sup>. The incidence of FBs in paranasal sinuses is increasing, which could be related to improved awareness, increased use of imaging, overuse of broad-spectrum antibiotics, increased endodontic treatment, or an aging population<sup>(3)</sup>.

Patients with FB typically present with nonspecific symptoms with various rhinological complaints that develop slowly<sup>(4)</sup>.

Symptoms are similar to chronic sinusitis, such as nasal obstruction, facial pain, or malodorous discharge<sup>(2)</sup>. Non-typical cases have been reported with severe symptoms such as seizures or cranial neuropathies<sup>(5)</sup>. FB sinusitis may also be discovered incidentally in imaging studies<sup>(1,2)</sup>. In one study, the maxillary was found to be most frequently involved, followed by the sphenoid sinus<sup>(6)</sup>. FB exhibits several distinctive features on CT imaging, including unilateral complete or partial opacification of the involved sinus, with focal areas of increased density. These areas may appear as foci containing calcifications<sup>(7)</sup>. Hyperostosis of the bony sinus walls or bone erosion may also be present<sup>(5)</sup>.

According to DeShazo et al's criteria, features such as unilateral sinus opacification, hyperostosis, and calcification foci are highly suggestive of FB infection<sup>(8)</sup>. MRI can help distinguish FB from other potential diagnoses, such as tumors or mucocles. Fungal infection may exhibit iso-hypointensity on T2-weighted images with surrounding hyperintense mucosa and non-enhanced hyperintensity on T1-weighted images<sup>(1,9,10)</sup>.

Surgical intervention is widely accepted as the preferred management approach for FB sinusitis<sup>(2)</sup>. Therefore, previously published cohorts on this condition did not include non-interventional arms of patients with asymptomatic FB lesions. This study aimed to examine the natural history and outcomes of incidental paranasal sinus FB findings on head imaging, cohort pooled from a large database of patients.

## Materials and methods

A retrospective study screening for patients who underwent imaging studies of the head, due to any indication, with incidental findings of sinus FB, during 2012- 2023, at our institution. First, a query of our imaging electronic database for the following imaging studies was conducted: computed tomography (CT) scans of the head and neck, total body CT, CT-angiography of the head and neck, magnetic resonance imaging (MRI), and positron emission tomography (PET), with a combination of one or more of the following phrases in the radiographic report: fungal infection, sinus mucosal thickening, hyperdensity of the

Table 1. Clinical and demographic data of 83 patients with incidental findings of FB.

Demographics	
Age at diagnosis, mean $\pm$ SD (range), yrs	78.33 $\pm$ 11.78 (34-98)
Follow-up, median (range), mo*	59.2 (10.2-178.8)
Female, n (%)	44 (53%)
Clinical parameters	
Comorbidities	
Environmental allergies	3 (3.6%)
Diabetes mellitus	35 (42.1%)
Hypertension	59 (71%)
Immunosuppressive medications	7 (8.4%)
Malignant disease and chemotherapy treatment	2 (2.4%)
Hemodialysis due to ESRD	2 (2.4%)
Suspected odontogenic origin	7 (8.4%)
Patients with presenting symptoms related to FB	4 (4.8%)
Headache	3
Headache	2
Rhinorrhea	1
Postnasal drip	2
Nasal obstruction	
Indication for 1st imaging study of the head	
Fall	28 (33.7%)
Suspected CVA	39 (47%)
Headache	7 (8.4%)
Other causes	9 (10.9%)
Endoscopic sinus surgery	5 (6%)
Status at the end of follow-up*	
Alive	49 (59%)
Dead from other cause	26 (31%)
Dead from unknown cause	8 (10%)

\* Follow-up was defined as the time interval between the first imaging study and the last day of data collection (Oct 1st, 2024). \*\* Physical examination by an otolaryngologist due to any indication, during the follow-up period. Abbreviations: FB, fungal ball; SD, standard deviation.

sinus or mucosa, fungal ball, mycetoma, aspergillosis, or aspergilloma. The pooled images were then screened by the authors for suspected presence of FB. All images suspected of evidence for FB were then further evaluated by the senior authors I.M., Y.S., and E.S to confirm or rule out the diagnosis based solely on imaging. The following diagnostic criteria (by De Shazo)<sup>(8)</sup> on CT were used to establish the diagnosis of FB: intra-sinus calcifications and partial or complete sinus opacification. Additional radiographic features on CT were evaluated: sinus wall bony sclerosis, and sinus wall erosion. Diagnostic criteria on MRI were sinus

Table 2. Radiographic data of 83 patients with fungal ball in this study.

Parameter		
Distribution of imaging studies among patients, n (%) *	CT Head	82 (99%)
	MRI Head	6 (7%)
	CTA	5 (6%)
	PET CT	2 (2.4%)
	CT sinuses	1
Sinus involved, n. (%)	Maxillary	42 (50.6%)
	Sphenoid	36 (43.4%)
	Ethmoid	2 (2.4%)
	Combined maxillary & ethmoid	2 (2.4%)
	Frontal	1 (1.2%)
Laterality	Unilateral FB, n. (%)	81 (97.6%)
	Bilateral FB, n. (%)	2 (2.4%)
CT characteristics, n (%)	Partial sinus opacification	48 (57.8%)
	Complete sinus opacification	35 (42.2%)
	Intrasinus calcifications	83 (100%)
	Sinus wall bony sclerosis	37 (44.5%)
	Sinus wall erosion	2 (2.4%)
MRI characteristics, n (%)	Hyper-signal intensity on T1WI and iso-hypo intensity on T2WI	6 (7.2%)

\* The number of patients that underwent each imaging study. Some patients had multiple imaging studies. Abbreviations: mo, months; T1WI, T1-weighted imaging; T2WI, T2-weighted imaging; CVA, cerebrovascular accident.

hyperintensity on T1-weighted images and iso-hypointensity on T2-weighted images.

Exclusion criteria were patients with other suspected or confirmed sinus pathologies: allergic fungal rhinosinusitis, acute or chronic invasive fungal sinusitis, foreign body (i.e., dental implants) in the sinuses, and benign or malignant sinonasal tumors.

FU time was defined as the period between the first imaging study with FB and last day of data collection (Oct 1st, 2024). The following demographic and clinical data were retrieved from the medical records: gender, age at diagnosis, immunosuppression status or malignancy, medical history, allergies, dental pathologies, sinuses involved and laterality, presenting symptoms and complications related to FB, otolaryngologic physical examination, endoscopic sinus surgery (ESS) and findings, overall and disease-specific mortality, and disease recurrence. Subgroup analyses were conducted between sphenoid and maxillary FBs. Patients with two or more consecutive imaging studies and a minimum interval of 6 months between the first and last study were selected for further analysis. When comparing the radiographic findings of these patients, dynamics were analyzed according to the following classification: no change, improvement, or worsening of imaging findings. The imaging parameters analyzed to determine dynamics were sinus opacification, sinus wall sclerosis, or bone erosion.

### Statistical analysis

The statistical analysis for this paper was generated using SAS Software, Version 9.4 (SAS Campus Drive, Cary, NC, USA). Continuous variables were presented by mean  $\pm$  standard deviation (SD) or median and interquartile ratio (IQR). Categorical variables were presented as (n, %). The normality of continuous variables was assessed using the Kolmogorov-Smirnov test. T-test was used to compare normally distributed continuous variables between study groups, Wilcoxon for non-normal continuous variables, and Fisher's exact test for categorical variables. Two-sided p-values less than 0.05 were considered statistically significant.

### Results

The computerized system query pooled 108,369 patients with imaging studies of the head during 2012- 2023, with a mean age of 63 years (64%  $\geq$  60 years, 36%  $<$  60 years) at the time of 1st imaging study.

After screening according to the search criteria for FB, 1,716 patients were identified, with a mean age of 66 years (4-100). Following scrutinized evaluation of their head images, only 83 had findings compatible with FB diagnosis according to our diagnostic criteria, giving a 0.075% incidental rate of FB in our cohort. The most common indications for the first head imaging study were falls and suspected cerebrovascular accidents (CVA).

### **Patients' characteristics**

The clinical and demographic data of patients are presented in Table 1. Overall, 44 (53%) females and 39 (47%) males were included, mean age  $78 \pm 11.78$  years, with a median FU time of 59.2 (10.2-178.8) months. The most common concomitant disease was hypertension (71%), followed by diabetes (54.2%) and immunosuppressive medications (8.4%). In a subgroup analysis of 45 immunocompromised patients (background of diabetes or immunosuppressive medications) versus 38 immunocompetent status patients, no significant difference was found in presenting symptoms, radiological findings, or surgical treatment.

A history of dental treatment was reported in 4 (4.8%) patients with either maxillary (three patients) or mixed maxillary-ethmoid FB (one patient). Two of those patients had radiographic findings of an exposed dental implant in the maxillary sinus, and one a periapical cyst. After reviewing the imaging studies of the other 38 patients with maxillary FB's, we noted the following dental pathologies in 3 (3.6%) more patients: radiographic oronasal fistula, filling material in the sinus floor post augmentation, and root canal material in the sinus floor.

Of 30 (36%) patients who had at least one visit to an otolaryngology clinic due to any indication during the FU period, only 4 (4.8%) had presenting symptoms that might have been associated with FB. The most common presenting symptoms were headache (three patients), followed by rhinorrhea (two patients), and postnasal drip (one patient).

### **Radiographic characteristics**

The most frequent imaging study of the head was CT (82 patients), followed by MRI (6 patients), and CT angiography 5 patients). Eighty-one patients (97.6%) had unilateral FB. The most involved sinuses radiographically were maxillary in 42 (50.6%) patients followed by sphenoid in 36 (43.4%) patients. CT characteristics were intra-sinus calcifications in all patients, and partial or complete sinus opacification in 48 and 35 patients, respectively. Additionally, sinus wall bony sclerosis was observed in 37 (44.5%), and sinus wall erosion in 2 (2.4%) patients. The radiographic characteristics of images are summarized in Table 2. No evidence of sinus wall bulging or ballooning, was seen in our patients.

The MRI characteristics in six patients were sinus hyperintensity on T1-weighted images and iso-hypointensity on T2-weighted images of the involved sinuses.

Characteristic CT findings of patients of right sphenoid sinus FB and right maxillary sinus FB are presented in Figure 1.

In a subgroup analysis comparing maxillary and sphenoid FB, amongst all clinical and radiographic parameters compared, the only significant parameters were more frequent presence of sinus wall bony sclerosis in sphenoid in comparison to maxillary FBs (26 vs. 11 patients, respectively,  $p < 0.001$ ).

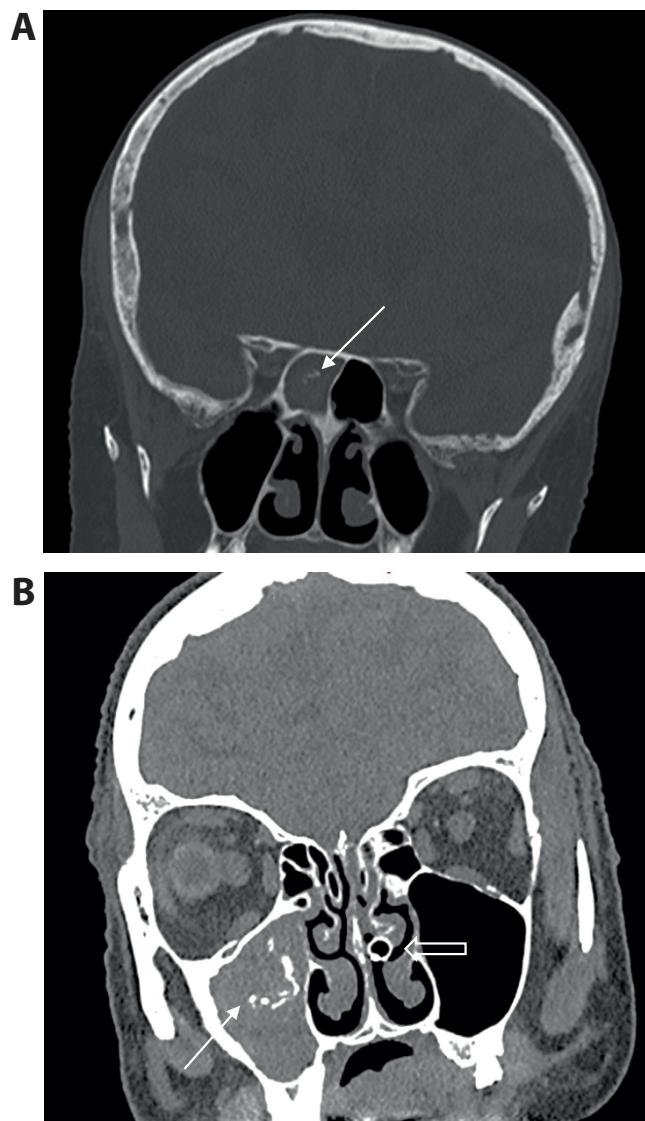


Figure 1. Characteristic findings in coronal CT scans of right sphenoid sinus FB (A) and right maxillary sinus FB (B). The figure presents a coronal CT scan of a patient with right sphenoid sinus FB (A), and of another patient with maxillary sinus FB (B). The radiological findings include complete sinus opacification, intrasinus calcifications (arrow), and sinus walls sclerosis. A nasogastric tube (open arrow) is seen in the left nasal cavity (B).

### **Clinical outcomes**

By the end of FU, 5 (6%) patients underwent functional endoscopic sinus surgery (FESS) to treat the involved sinus. The indications for surgery were:

1. Unilateral Headache/ Facial pain (2 patients), accompanied by nasal blockage and rhinorrhea (1 patient).
2. Nasal blockage and rhinorrhea (1 patient)
3. Incidental finding in a patient had an urgent FESS due to severe epistaxis, which did not resolve with nasal packing. Before surgery, a sinus CT was done, which gave an incidental finding of sphenoid FB with suspected dehiscence of

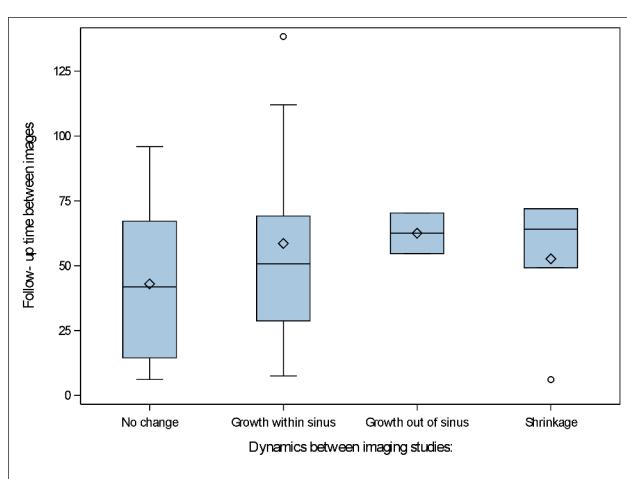


Figure 2. Dynamics amongst imaging studies of 49 patients with two consecutive imaging studies. The box plot describes the dynamics between the first and last CT of the patients during a median follow-up of 50.33 months. Most patients had no change (29, 59.2%) or even improvement (5, 10.2%) in their radiographic characteristics.

the lateral sphenoid sinus wall adjacent to the internal carotid artery. Thus, in addition to bleeding control from the posterior septum, a wide sphenoidotomy was performed with clearance of mucopurulent clay-like material. No intra or postoperative complications were reported.

The surgical findings of these patients were mucopurulent clay-like material compatible with FB. One patient with maxillary sinus FB had also inflammatory polyps in the sinus, however no polyps were seen in the other cases.

By the end of FU, one patient had recurrent FB in the maxillary sinus 5 years after their first surgery and had undergone a revision ESS. The other four patients had no recurrence of symptoms or complications.

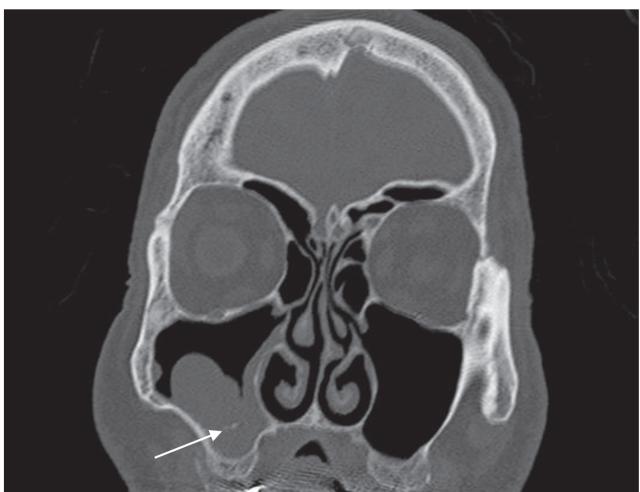
The remaining 78 (94%) patients with FB did not receive any treatment during FU, without any reported morbidity or complications. After a thorough screening of medical registries, none of these patients had any reported visits to otolaryngologic clinics or hospital admissions with symptoms or signs that could be explained by FB. No visual symptoms attributed to FB were reported.

At the end of the study, 49 (59%) patients were alive, and 34 (41%) were dead of other causes. No known mortality was attributed to FB.

#### Imaging dynamics over time

Forty-nine (59%) patients had two consecutive imaging studies with a minimum of 6 months interval between the first and last imaging, and a median FU of 50.3 (6.1-138.37) months. The radiological findings of these patients are presented in Table 3. When comparing characteristics of the first and last imaging

A



B

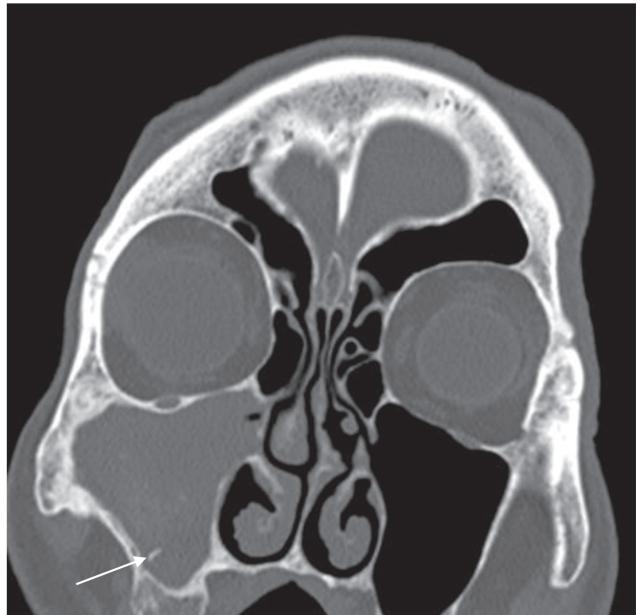


Figure 3. Representative coronal CT scans of right maxillary sinus FB with worsening radiological findings during 111-month interval. The figure presents worsening radiological findings between the initial (A) and last (B) scans of a patient with right maxillary sinus FB, that include intrasinus calcifications (arrow), complete opacification and sinus wall sclerosis.

scans of patients, the dynamics in radiological findings were as follows: no change (59.2%), worsening opacification within the sinus (26.5%) or out of the sinus (4.1%), and improvement (10.2%).

No differences were found between the first and last imaging scans concerning the other radiographic characteristics, and sinus wall sclerosis.

Further analysis did not reveal any significant clinical or radiolo-

Table 3. Radiological findings among 49 patients with 2 consecutive imaging studies.

Parameter	n (%)
Time interval between images [mo], median (range) *	50.33 (6.1- 138.37)
<b>Sinus involved, n (%)</b>	
Maxillary	23 (47%)
Sphenoid	22 (45%)
Ethmoid	1 (2%)
Maxillary & ethmoid	2 (4%)
Frontal	1 (2%)
Unilaterality, n (%)	49 (100%)
<b>Imaging characteristics, n (%)</b>	
Partial sinus opacification	30 (61.2%)
Complete sinus opacification	19 (38.8%)
Intrasinus calcifications	49 (100%)
Sinus wall bony sclerosis	27 (55.1%)
Sinus wall erosion	1 (2%)
<b>Dynamics in imaging findings between first and last imaging studies, n (%)**</b>	
No change	29 (59.2%)
Increased opacity within the sinus	13 (26.5%)
Increased opacity out of the sinus	2 (4.1%)
Decreased opacity	5 (10.2%)

\* The time interval between patients' first and last imaging study during follow-up period. \*\* Dynamics in CT findings while comparing patients' first and last CT scans with a minimum time interval of 6 months.

gical predictors for worsening or improving radiological findings of patients during FU.

The dynamics of CT findings are presented in Figure 2. Out of the five patients diagnosed with FESS, one had radiographic signs of worsening of imaging findings within the sinus, one showed improvement, and three had a single imaging study. In a subgroup analysis of 25 patients with maxillary and 22 with sphenoid sinus involvement and two consecutive imaging studies, no significant differences were found in the dynamics of imaging findings ( $p=0.273$ ).

Worsening imaging findings of a right maxillary sinus FB during 111-months interval are presented in the initial and last coronal CT scans of the same patient (Figure 3).

## Discussion

This study aimed to examine the natural history of paranasal sinus FB, diagnosed as an incidental finding on imaging, in a cohort of patients pooled from a large database. To the best of our knowledge, this is the first study to examine a non-interventional cohort of patients with FB.

We noticed that the majority (79, 95%) of patients remained asymptomatic during a mean FU of 59.2 (4.9 years) months, without known morbidity or complications. The minority of symptomatic patients plus an additional patient with severe sphenoid sinus wall erosion were operated on, with a complete resolution of their symptoms. Sinus wall sclerosis was the only significant factor more common in sphenoid FBs, in comparison to maxillary FBs. The 34/49 (69.4%) patients had either no radiographic change or improvement of CT findings during a median time interval of 50 months between images, while 30% had worsening of findings of increased opacification.

The mean age of patients with FB in this study was 78.3 years, older than the 52-65 years reported in large retrospective studies of FB patients <sup>(1,14-19)</sup>. We presume this is associated with that our imaging database search was done in a tertiary referral center, with a larger number of elderly people referred to our hospital (mean age of the entire cohort was 63 years) due to suspected CVA, head trauma due to falls, or other comorbidities.

Female preponderance in our cohort correlates with other studies <sup>(15)</sup>.

Hypertension was the most common (77%) concomitant disease in our cohort while diabetes was the second (42.1%). Although other studies mentioned different comorbidities' rates, no correlation can be drawn between them and FB development <sup>(3,16,17)</sup>. One reason is that these comorbidities pertain to an aging population and other demographic factors that vary between cohorts.

Of 7 (8.4%) patients in our cohort with a possible odontogenic etiology for maxillary FB, four reported a dental procedure before FB diagnosis and three had dental pathological findings on CT. Endodontic treatment with the development of an anaerobic environment was suggested to be a possible contributing factor for FB <sup>(1)</sup>. According to some reviews, 84-86% of patients with maxillary FB have had prior endodontic treatment. According to one theory, FB might be triggered by the passage of a foreign body or dental sealers containing zinc oxide into the sinus <sup>(6,18)</sup>. However, the number of patients with possible odontogenic etiology in our cohort was smaller as compared to those studies, probably due to a lack of documentation due to treatment outside of our institution.

The majority (95%) of patients in our study were asymptomatic during a mean FU of 59.2 months. The most common indications for head imaging were falls and suspected CVA in 80.7% of cases. This contrasts with a study <sup>(2)</sup> of 538 FB patients treated surgically, where most patients (92-94%) were symptomatic. The most common symptom was headache (70%) followed by post-nasal drip and nasal obstruction (60%), and rhinorrhea (53%). In maxillary FB, postnasal drip, nasal obstruction, and rhinorrhea were more common, while in sphenoid FB headache was more frequent <sup>(1)</sup>. Similarly, headache was the most common symptom (79%) of sphenoid FB in another study, in which only

9% of patients were asymptomatic. Notably, 7.8% of patients in that study had visual symptoms<sup>(15)</sup>. However, the patients in those studies were selected based on surgical intervention, in contrast to our study. Interestingly only 4 (4.8%) patients in our study presented with symptoms attributed to FB and were subsequently operated on. No visual symptoms or neurologic manifestations, apart from headache, were noted during FU. One additional patient with sphenoid FB and significant lateral sphenoid wall bony erosion was operated on when already in the operating room for epistaxis control.

By the end of the FU, 49 (59%) patients were alive, and 34 (41%) dead, none of them due to a known complication of FB. The high mortality rate may be attributed to the elderly population of the study cohort (mean age 78 yrs), as well as presence of comorbidities, such as hypertension, diabetes, ischemic heart disease, and CVA.

The most common imaging study used FB diagnosis in this study was head CT scan, followed by MRI. This correlates with other studies, which used CT scan as imaging of choice for FB diagnosis<sup>(4,15,17)</sup>.

One of the clinicopathological criteria for diagnosis of sinus FB, proposed by DeShazo, was radiologic evidence of sinus opacification with or without associated flocculent calcifications<sup>(8)</sup>. Both sinus opacification, partial or complete, and intrasinus calcifications were absolute criteria for FB diagnosis in this study, with a specificity of 99-100%. Similarly, they were the two most common CT findings in other studies (50-80% of cases)<sup>(3,19)</sup>. Additional CT characteristics in our study cases were bony sclerosis of sinus walls (44.5%), and sinus walls erosion (2.4%). Those characteristics were evaluated after a thorough observation of the coronal, axial, and sagittal planes of the CT scans.

In comparison, sclerosis of sinus wall, termed osteitis, was reported in 37-61% and bone erosion in 4-21% of FB cases in other studies<sup>(3,6,8)</sup>. Interestingly, sinus wall bony sclerosis was significantly more prevalent in sphenoid, in comparison to maxillary FB. Bony sclerosis, erosion or expansion are part of bone remodeling in chronic inflammation, as reported in CRS.<sup>(20)</sup> Although sinus wall bulging may occur from FB, no evidence of it was seen in our cohort<sup>(6)</sup>.

In our study, the maxillary sinus was most frequently involved (50.6%) as compared to the sphenoid sinus (43.4%). In comparison, other studies on operated patients reported maxillary sinus involvement in 70-94% of cases, sphenoid sinus in 4-18%, ethmoid in 0.6-3%, and frontal in 2% of cases<sup>(10,19,21)</sup>. We did not find a significant difference between the prevalence of presenting symptoms between maxillary and sphenoid FB; however, this may be due to the low number of symptomatic patients in our cohort.

We identified 81 (97.6%) patients with unilateral FB, which is similar to previous reports in the literature<sup>(1,4,15,16)</sup>.

When investigating the natural history of these FB findings, the majority (69.4%) of patients with two consecutive imaging studies had either no radiographic change or showed improvement of CT findings during a median time interval of 50 months. Worsening of sinus opacification within or out of the sinus did not correlate with presenting symptoms or surgical intervention. In addition, we did not find a significant predictor for worsening or improvement of imaging findings over time in our cohort. We are unaware of other studies in the current literature that reported similar dynamics of radiographic findings of FB. A possible reason is that cohorts had surgical treatment with resolution of clinical signs and symptoms.

By the end of FU, 78 (94%) patients with FB had not received any treatment during FU or reported morbidity or complications. This unique observation has not been previously reported. According to other studies, surgical treatment for FB was proven to be efficient in the majority of patients, with a low rate of recurrences (1-2%)<sup>(1)</sup>.

The surgical findings in our study included clay-like material, with or without mucopurulence that is characteristic of FB. DeShazo et al. proposed it as one of the clinicopathologic criteria for the diagnosis of FB, and one study described it as a pathognomonic finding<sup>(8)</sup>. Histologically, the fungal material comprises dense collections of fungal hyphae in most cases, without signs of angioinvasion<sup>(1,6)</sup>. Unlike the maxillary sinus, the sphenoid sinus is surrounded by critical structures such as the pituitary gland, cavernous sinuses, optic nerves, and internal carotid arteries. Since chronic inflammation can lead to bone remodeling and erosion, these structures may be at risk if left untreated. This risk can be caused by various etiologies, such as bacterial sinusitis, mucocele, or neoplasm. Although we did not find a complication of sphenoid FB in asymptomatic patients during a mean FU of 5 years in our cohort, it may pose a risk if left untreated for a longer time. Headache and visual complications, such as decreased visual acuity and diplopia, were reported in a systematic review of isolated sphenoid opacification<sup>(22)</sup>. In addition, anecdotal reports of skull base erosion and internal carotid artery thrombosis from a sphenoid FB were published<sup>(23)</sup>. Unilateral sinus opacification should raise a suspicion of an infectious cause, as well as of a benign or malignant neoplasm, and warrants a thorough evaluation. In one review, neoplasia presented in 18% of incidental isolated sphenoid and maxillary sinus opacification<sup>(22)</sup>. Decision-making regarding the ideal treatment should be based on clinical diagnosis, physician's preference, and patient's will. Benefits should be weighed against the risks of surgery and anesthesia, especially for critically ill or elderly people, when deciding if to operate.

### Limitations

These include its retrospective character, relatively small number of surgically treated patients in comparison to other studies,

possibly incomplete data relying on self-reported symptoms that might be affected by the patient's cognitive or physical state, and as not all patients were evaluated by an otolaryngologist who would have been more aware of the nature of this disease. In addition, the diagnosis of FB was based on radiographic findings, rather than on surgical findings, since most did not undergo surgery. Lastly, our cohort represents a group of patients who were referred to a tertiary center from the community, and therefore may include older patients with more comorbidities, and may not represent the entire population of FB patients. Nine patients (10.8%) in our cohort had various degrees of dementia as reported in their medical records, however we do not have the data on whether these patients were or were not able to speak of their symptoms. We did not limit our search to age or comorbidities, and the prevalence of dementia is correlated with the mean age of the cohort.

## Conclusion

In this study, the natural history of incidental paranasal FBs in a large cohort of patients was examined. During a mean duration time of 5 years, most patients were elderly and remained asymptomatic without disease-specific morbidity. Thus, upfront surgical intervention for asymptomatic paranasal FB in elderly fragile patients, who may be at a higher risk for general anesthesia may not be mandatory. Clinical and imaging a follow-up

can be a reasonable alternative for these patients with special attention in sphenoid fungal balls for worsening symptoms or imaging findings. Further studies on larger cohorts of patients, including younger patients, and with longer follow-up durations are warranted to corroborate these findings.

## Ethical approval and consent to participate

This study was approved by the Institutional Research Ethics Committee (RMC-055021). Patients' consents were waived due to the retrospective character of the study.

## Conflict of interest

The authors declare no potential conflicts of interest.

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This research received no specific grant or funding.

## Authors' contributions

IM: study design, search, data collection, data analysis, drafting and revising the article. YS: search, data collection, and revising the article. TZ: search, data collection. SE: search, data collection. IY: search, data collection. TS: data collection, and data analysis. ES: conception, study design, data analysis, revising and final approval of the article.

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