



Combining sinus plain film and sinus ultrasound as a screening tool for maxillary fungal sinusitis

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Abstract

Background: Early identification of fungal sinusitis remains a challenge. Previously, we observed a high false negative rate of using A-mode ultrasound to diagnose maxillary fungal sinusitis. This study aims to assess the accuracy of the diagnosis of fungal maxillary sinusitis using sinus plain film and ultrasound.

Methods: The screening criteria is defined as the combination of a positive sinus plain film and a false negative sinus ultrasound. We retrospectively reviewed preoperative imaging of patients with fungal sinusitis and unilateral bacterial sinusitis of the maxillary sinus undergoing functional endoscopic sinus surgery from May 2013 to December 2019 in our hospital and evaluated the diagnostic performance of this screening method.

Results: Forty-eight patients were included. Twenty-two and 26 patients were diagnosed with fungal sinusitis and bacterial sinusitis, respectively. Sixteen patients (72.7%) with fungal sinusitis presented with a false negative sinus ultrasound and met our screening criteria for fungal sinusitis. The screening criteria reached significance in the receiver operating characteristic curve analysis ($p < 0.001$). The area under the curve was 0.829. The sensitivity, specificity, and accuracy are 72.7%, 93.2%, and 88.4%, respectively.

Conclusion: A high false negative rate of sinus ultrasound in patients with fungal sinusitis was found. A positive sinus plain film combined with a false negative sinus ultrasound can potentially become an easy and cost-effective screening tool for diagnosing fungal maxillary sinusitis before consideration of computed tomography scanning.

Keywords: Area under curve; Maxillary sinusitis; ROC curve; Tomography; X-rays

1. INTRODUCTION

There is an increasing incidence of fungal sinusitis in recent decades, possibly due to increased recognition and early diagnosis, antibiotic overuse, and increased immunocompromised hosts.^{1,2} Currently, fungal sinusitis accounts for 10% to 30% of chronic rhinosinusitis treated with surgery.^{1,3,4} Mycotic paranasal infections can be classified broadly into noninvasive and invasive forms. The noninvasive forms include fungal ball (mycetoma) and allergic fungal rhinosinusitis. The invasive forms comprise acute, chronic, and chronic granulomatous fungal sinusitis. The most common type of fungal sinusitis is a fungal ball, with 79% to 94% of cases occurring in the unilateral maxillary sinus.^{1,5}

Patients with fungal sinusitis may have subtle or nonspecific presentations similar to chronic rhinosinusitis, and the

endoscopic exam is neither sensitive nor specific.^{1-3,5} Thus the initial diagnosis of fungal sinusitis is usually made on computed tomography (CT) scan, with reported sensitivity and specificity of 62% and 99%, respectively.^{1,2} MRI is indicated in invasive diseases with the involvement of orbit and skull base.^{1,6-8} On CT scan, opacification of the unilateral sinus with intralacinal hyperdensity or calcification is the typical finding of the fungal ball.^{6,7,9} Other significant features include erosion of the sinus inner wall, sclerosis of the sinus lateral wall, heterogeneous soft tissue density, and absence of air-fluid level.⁹ However, the use of a CT scan is limited by its high cost and radiation exposure to patients. It is usually done when there is no response to medical treatment during the management of chronic rhinosinusitis. Due to the above, early and rapid diagnosis of fungal sinusitis remains a great challenge.^{1,5}

A-mode ultrasound and sinus plain film are two readily available, noninvasive imaging tools to diagnose bacterial maxillary sinusitis. Both exams have variable but generally moderate sensitivity and specificity according to published data.¹⁰⁻¹⁹ A previous study in our hospital revealed that the diagnostic rates of sinus ultrasound and sinus plain film were 78.4% and 75.6%, respectively.¹³ Although they are widely used in daily practice for the investigation or follow-up of bacterial sinusitis, there has been no study addressing the use of these imaging modalities in fungal sinusitis. In our clinical observation, a high percentage of patients with fungal maxillary sinusitis presented with a positive sinus plain film and a false negative sinus ultrasound. Hence, we

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proposed the screening criteria for the diagnosis of fungal maxillary sinusitis by using sinus ultrasound and sinus plain film.

Our study aims to early identify fungal maxillary sinusitis simply and cost-effectively, to facilitate definite imaging diagnosis and prompt surgical treatment in these patients.

2. METHODS

2.1. Clinical data

The subjects of this study consisted of patients with fungal sinusitis and unilateral bacterial sinusitis of the maxillary sinus. They underwent functional endoscopic sinus surgery from May 2013 to December 2019 at the Taipei Veterans General Hospital after failing medical therapy, including oral antibiotics. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board of the Taipei Veterans General Hospital. Data regarding demographics, presentation, endoscopy, sinus plain film, sinus ultrasound, CT scan, and pathology were retrieved. Patients with a diagnosis of sinonasal neoplasm, bilateral disease, or unspecified pathology were excluded. The screening criteria for fungal maxillary sinusitis were defined as a combination of a positive sinus plain film and a false negative sinus ultrasound. We also evaluated the contralateral maxillary sinus, which, per inclusion criteria, consisted of healthy sinuses based on intraoperative findings and analyzed it as part of the control group.

We routinely sample mucosal tissue and cultures within the infected maxillary sinus during surgery. Bacterial culture and fungal culture were obtained. The mucosa was stained with hematoxylin and eosin and was examined under microscopy. Gomori Methenamine-Silver stain was also performed for the evaluation of fungal elements. Fungal sinusitis was pathologically diagnosed by the presence of fungal colonies in the specimen. Invasive fungal sinusitis was defined by tissue invasion with aggregates of fungal hyphae within the respiratory mucosa, blood vessels, or bone.

2.2. Diagnostic tools

Endoscopy

Rigid sinonasal endoscopy with a 4-mm 0-degree telescope was performed in all patients in the outpatient clinic after local anesthesia with 2% xylocaine and 1:5000 parts epinephrine spray. The middle meatus and ostiomeatal complex were carefully examined. The endoscopic findings were classified into four categories: normal, mucopus, polyps, and fungal ball.

Sinus plain film

The standard radiography of the paranasal sinus included three projections: occipitofrontal, occipitomeatal, and lateral views.

In this series, we only examined the maxillary sinus under the occipitomeatal view (Waters' view). Evidence of sinusitis is made by one of the following findings: total opacification, air-fluid level, or mucosal thickening measuring more than 5 mm within the maxillary sinus.

Sinus ultrasound

The patients were instructed to sit upright with their neck slightly flexed. A-mode ultrasonography was performed with the Sinus Echoscope DIGITAL 5 (Happersberg Otopront GmbH, Hohenstein, Germany) using a 10-mm transducer and a frequency of 4.25 MHz. The ultrasound transducer is gently placed over the cheek skin overlying the maxillary sinuses. Although the relationship of the back wall echo and mucosal thickening has been documented,²⁰ it is still very difficult to precisely measure the mucosal thickness by sinus ultrasound alone considering the variation of skin and soft tissue thickness in each individual.^{21,22} As a result, we defined the presence of a back wall echo with distance ≥ 3.5 cm as a positive sinus ultrasound, which is the most traditional definition,²⁰⁻²² indicating fluid retention commonly seen in the bacterial sinusitis. On the contrary, a "false negative ultrasound" was defined as the absence of a back wall echo with distance ≥ 3.5 cm but was proved to be a maxillary sinusitis intraoperatively afterward. An example of interpretation was presented in Fig. 1.

All patients received the above tests and a CT scan preoperatively.

2.3. Data analysis

The results of all maxillary sinuses were calculated independently. Statistical analysis was performed using SPSS (version 21.0; IBM Corp., Armonk, NY, USA). Comparisons of means and proportions were tested with the independent *t* test and Chi-square test/Fisher's exact test. A *p* value of 0.05 was considered statistically significant. The sensitivity, specificity, accuracy, positive/negative predictive value, and positive/negative predictive likelihood ratio were calculated. Receiver operating characteristic (ROC) analysis was performed to evaluate the diagnostic ability of the screening criteria for fungal maxillary sinusitis.

3. RESULTS

A total of 48 patients (23 males and 25 females) were included. Twenty-two and 26 patients were diagnosed as fungal maxillary sinusitis and bacterial maxillary sinusitis, respectively. There were 6 patients diagnosed with chronic invasive fungal sinusitis. Among patients with bacterial sinusitis, 14 cases were caused by odontogenic infection. One patient with fungal sinusitis had simultaneous odontogenic sinusitis in the opposite maxillary

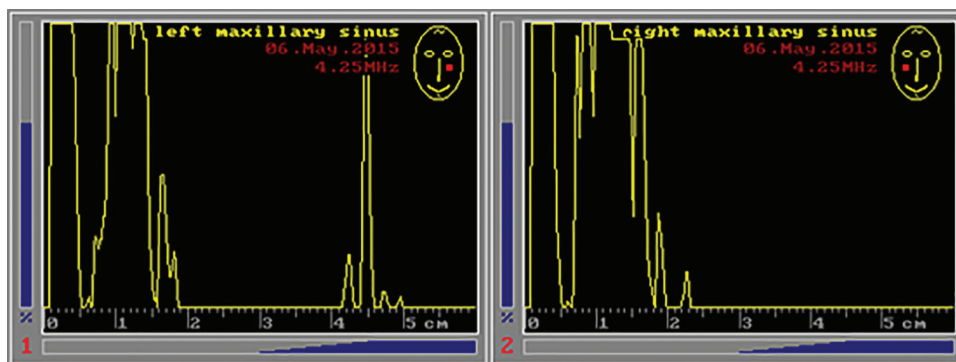


Fig. 1 Interpretation of sinus ultrasound. In this example, A-mode ultrasonography was performed over bilateral maxillary sinus. The result of sinus ultrasound of left maxillary sinus was positive, presenting a back wall echo with distance ≥ 3.5 cm. On the contrary, the result of right maxillary sinus was negative.

sinus. Forty-three (89.6%) patients received sinus plain film and sinus ultrasound within two weeks of surgery.

The mean age of this study population was 51.6 years (range, 18–92 years). 52.1% of patients were female, and 56.3% of patients had unilateral left-sided sinusitis. Gender and the side of diseased sinus showed no significant difference between patients with fungal sinusitis and bacterial sinusitis. However, patients with fungal sinusitis were significantly older than patients with bacterial sinusitis (mean age, 60.8 and 43.8 years, respectively; 95% CI, 7.695–26.158]; $p = 0.001$). A trend toward a higher prevalence of comorbidities (eg, diabetes, cardiovascular disease, cancer) was also observed in patients with fungal sinusitis (Table 1). The patients were subdivided into two age groups: age <50 years and age ≥50 years. There was no significant difference between each imaging finding and the positivity of the screening criteria between the two age groups.

Patients with fungal maxillary sinusitis presented with purulent rhinorrhea (n = 18, 81.8%), postnasal drip (n = 9, 40.9%), nasal obstruction (n = 7, 31.8%), cough (n = 4, 18.2%), and headache or facial pain (n = 2, 9.1%). Three (13.6%) patients were asymptomatic (Fig. 2A). Preoperative endoscopy revealed mucopus in 16 (72.7%) patients. Polyps and fungal ball were found in three (13.6%) and two (9.1%) patients, respectively. Three (13.6%) patients had normal mucosa (Fig. 2B).

Among the fungal sinusitis group, all patients had complete opacification of unilateral maxillary sinus on Waters' view, with 100% sensitivity. Sixteen patients (72.7%) presented with a false negative sinus ultrasound and met our screening criteria for fungal sinusitis. Among the bacterial sinusitis group, 25 patients (96.2%) had a positive sinus plain film, and 21 patients (80.8%) had a positive sinus ultrasound. Sinus plain film and ultrasound had consistent results in 20 (76.9%) patients. Only 5 patients (19.2%) fit the screening criteria. There was no significant difference in the sensitivity of sinus plain film between two groups ($p = 0.353$). On the contrary, comparing fungal sinusitis to bacterial sinusitis, sinus ultrasound had a compelling false negative rate and the screening criteria possessed a significantly high sensitivity (both $p < 0.001$; Table 2).

One patient with left fungal sinusitis had simultaneous right bacterial sinusitis, which improved after antibiotic treatment. Thus, the status of the right maxillary sinus of this patient was excluded from the healthy sinus control group. In the contralateral healthy sinus group, 1 patient (2.1%) had a false positive sinus plain film, and 2 patients (4.3%) had a false positive sinus ultrasound. No patient met the screening criteria. As we incorporated the results of bacterial sinusitis and contralateral healthy sinus as the control group, the screening criteria still

Table 1

Comparison of demographic data between fungal sinusitis and bacterial sinusitis

	All patients (n = 48)	Fungal sinusitis (n = 22)	Bacterial sinusitis (n = 26)	p
Age (mean ± SD)	51.6 ± 17.8	60.8 ± 13.1	43.8 ± 17.8	0.001
Gender (male:female)	23:25	10:12	13:13	0.753
Laterality (left:right)	27:21	14:8	13:13	0.343
Comorbidity	19 (39.6%)	12 (54.5%)	7 (26.9%)	0.051
Diabetes	2	2	0	
Cardiovascular disease	15	9	6	
Cancer	6	5	1	
Renal disease	2	1	1	
Autoimmune disorders	3	1	2	

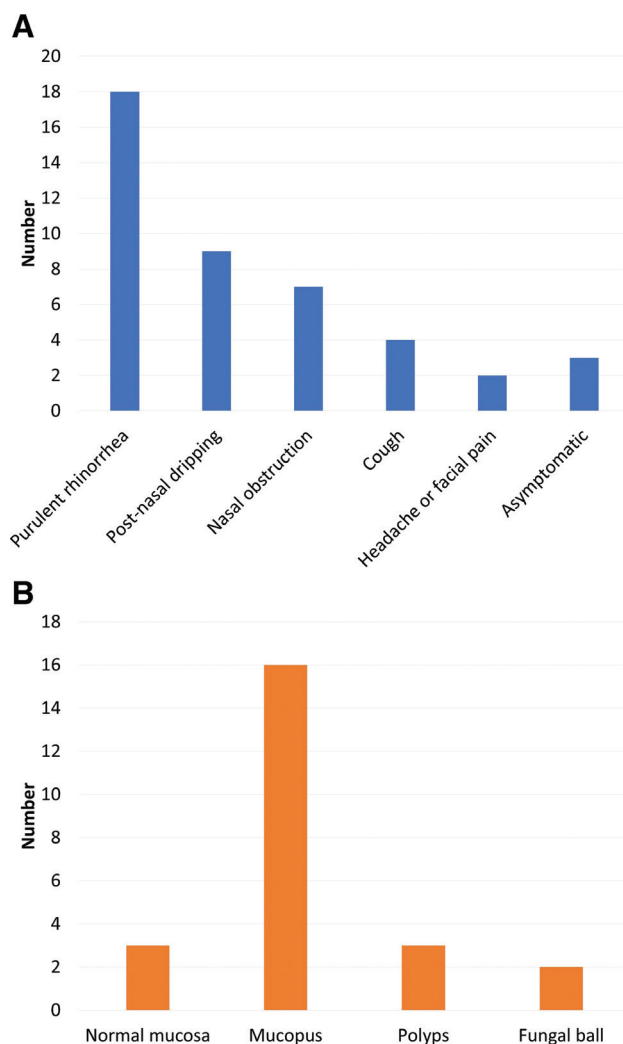


Fig. 2 Clinical presentation and endoscopic findings of fungal maxillary sinusitis. A, Clinical presentation of fungal maxillary sinusitis. B, Endoscopic findings of fungal maxillary sinusitis.

had a significantly high sensitivity in fungal sinusitis as predicted ($p < 0.001$; Table 2).

The diagnostic ability of the screening criteria reached significance in the ROC curve analysis ($p < 0.001$). The area under the curve was 0.829. The sensitivity, specificity, and accuracy were 72.7%, 93.2%, and 88.4%, respectively. The positive/negative predictive value was 76.2%/91.9%, and the positive/negative predictive likelihood ratio was 10.62/0.29 (Fig. 3).

4. DISCUSSION

Older individuals are traditionally thought to be more vulnerable to fungal sinusitis, with a female predominance for the unilateral fungal ball.^{1,5,7} We observed that patients with fungal sinusitis were significantly older than patients with bacterial sinusitis, while there was no obvious gender difference (Table 1). The trend of a higher percentage of comorbidities in patients with fungal sinusitis can be explained by the age difference. However, further analysis of older and younger age groups revealed that age does not influence the imaging results or the screening criteria.

The clinical presentation of fungal sinusitis varies widely. Most patients had nonspecific symptoms similar to other types of chronic rhinosinusitis while some can be completely asymptomatic. It has

Table 2
Comparison of diagnostic tools

	Fungal sinusitis (n = 22)	Bacterial sinusitis (n = 26)	Healthy sinus (n = 47*)	Bacterial sinusitis + healthy sinus (n = 73)	p (fungus vs bacteria)	p (fungus vs bacteria + healthy)
Sinus plain film (+)	22 (100%)	25 (96.2%)	1 (2.1%)		0.353	
Sinus ultrasound (+)	6 (27.3%)	21 (80.8%)	2 (4.3%)		<0.001	
Screening criteria: sinus plain film (+) and sinus ultrasound (-)	16 (72.7%)	5 (19.2%)	0 (0%)	5 (6.8%)	<0.001	<0.001

*One patient with left fungal sinusitis had simultaneous right bacterial sinusitis, which improved after short term of antibiotic treatment. Hence, the result of right maxillary sinus of this patient was excluded from the healthy sinus control group.

been reported that 13.2% to 20% of patients with fungus balls had no symptoms and were diagnosed incidentally by imaging unrelated to sinonasal complaints.¹ In our study, the most common symptom of fungal maxillary sinusitis is purulent rhinorrhea, followed by postnasal drip and nasal obstruction. 13.6% of the patients were asymptomatic. Endoscopy of the middle meatus can reveal anything from normal mucosa to pathologic features such as mucopus, crusting, polyps, and edema. The only explicit finding of endoscopy, which is more confirmatory of the diagnosis, is the presence of fungal ball, described as “cheesy” or “clay-like” viscid mucin in the sinus or ostiomeatal complex, which is mostly encountered intraoperatively.^{1,2} In our study, the most common endoscopic feature is mucopus, and 13.6% of patients had a normal endoscopic exam. The fungal ball was only detected endoscopically in 9.1% of patients preoperatively.

Sinus plain films, especially Waters’ view, is an older imaging modality for maxillary sinusitis. It is quick, safe, inexpensive, and noninvasive. According to a systemic review, the sensitivity and specificity of this modality in making the diagnosis of acute maxillary sinusitis were 87% and 89%, respectively.¹⁰ Recently, there is emerging evidence suggesting that using deep learning models in the diagnosis of maxillary sinusitis on Waters’ view radiograph was associated with superior accuracy.^{23–26} In our study, we found that sinus plain films had very high sensitivity in

diagnosing both fungal and bacterial maxillary sinusitis (100% and 96.2%, respectively). There are two possible reasons. First, we only included unilateral maxillary sinusitis in this study. This might increase the sensitivity since a comparison of the contralateral healthy side makes the interpretation easier. Second, the calcified materials in fungal sinusitis may enhance the opacities on radiograph, making it easier to detect.

In our study, all patients with fungal sinusitis presented with total opacification of unilateral maxillary sinus on Waters’ view. Focal hyperdensity within the hazy sinus was sometimes seen, which is reported in 25% to 50% of fungal balls.¹ Nonetheless, it is a nonspecific feature shared by bony structures, foreign bodies, or dental prosthesis. Interestingly, no air-fluid levels were observed. We also found that 90.1% of patients with fungal sinusitis had no air-fluid level (either on axial or sagittal view) on CT scan. It has been noted that 97.9% of maxillary fungal balls presented with the absence of air-fluid level on CT scan, significantly more than in bacterial sinusitis.⁹ Thus, the presence of air-fluid levels may serve as a negative predictor of fungal sinusitis. Yet, total opacification on sinus plain films occurs in both fungal sinusitis and bacterial sinusitis. Similarly, this modality usually does not discriminate sinusitis from other diseases like polyps or tumors. Furthermore, anatomic variations, such as maxillary sinus hypoplasia, may confound accurate interpretation.^{12,19} According to the American College of Radiology, plain sinus films alone give a high percentage of inaccurate results and should be interpreted with caution.¹²

A-mode ultrasound is another imaging modality for detecting maxillary sinusitis. This exam is quick, safe, inexpensive, noninvasive, and without radiation exposure. The sensitivity and specificity in the diagnosis of acute sinusitis were reported as 85% and 82%, respectively, which is slightly lower as compared to sinus plain films.¹⁰ In our patients with fungal sinusitis, 86.3% of patients had calcifications within the maxillary sinus on CT scan. Of these patients, 78.9% had negative ultrasound findings. Among the only 3 patients who had no calcification on CT scan, 2 (66.7%) of them had a positive sinus ultrasound. We explain that the more calcified and heterogeneous material within the sinus, the more likely the ultrasound would be interpreted negatively, as the sound wave would be less effectively transmitted. This phenomenon provides the ability of ultrasound to separate fungal sinusitis from bacterial sinusitis.

It has been shown that the addition of sinus plain film to ultrasound increases the sensitivity in the detection of acute maxillary sinusitis.¹¹ The two exams have moderate consistency, reflecting the fact that they have very different mechanisms.¹³ In patients with bacterial sinusitis, 76.9% of cases had concordant results in sinus plain film and ultrasound. However, we observed an unusually low consistency in patients with fungal sinusitis, and a surprisingly high false negative rate of ultrasound was found. The screening criteria were proposed based on this clinical observation. The screening criteria have good discrimination ability, fair sensitivity, and excellent specificity for fungal maxillary sinusitis. It takes advantage of the extremely high sensitivity of the sinus plain film and the specificity of ultrasound. The results of our

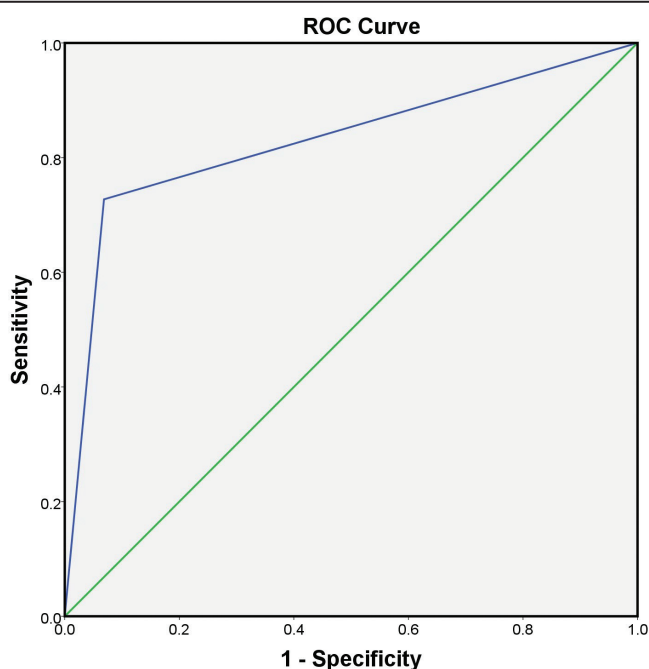


Fig. 3 Receiver operating characteristic (ROC) curve of the screening criteria for fungal maxillary sinusitis. The area under the curve is 0.829 ($p < 0.001$; 95% CI, 0.713–0.946).

study revealed that the screening criteria can not only be used to discriminate fungal sinusitis and bacterial sinusitis but also as a screening tool to determine whether the sinuses are healthy. Both fungal sinusitis and bacterial sinusitis can present total opacity on sinus plain film. If the patient has a finding of total opacity under Waters' view and a negative sinus ultrasound simultaneously, he/she has a great chance of getting a fungal sinusitis, as the images fit the screening criteria we proposed in this study.

A sinus plain film and a sinus ultrasound together cost about \$17 in our hospital, which is much cheaper than a CT scan (\$198). Even when endoscopy (\$52) is added, the total cost is still much lower. These exams can screen patients with very limited radiation exposure. For instance, skull radiographs typically deliver 0.1 mSv of radiation, as compared to 0.7 mSv for CT sinus. Either a sinus plain film or a sinus ultrasound takes less than 10 minutes to be done in the outpatient setting, which is very convenient and time-saving compared to a CT scan. Many patients with fungal sinusitis experience a long symptomatic period before a correct diagnosis can be made. This results in a substantial economic and medical burden, not mentioning the possible impact on the quality of life and antibiotic resistance. Furthermore, the progression of the disease and devastating complications may sometimes occur if fungal sinusitis is left untreated. As a result, any solution that can readily identify

fungal sinusitis earlier has clear clinical benefits. Our screening criteria can potentially become a simple and cost-effective screening tool before consideration of CT scanning.

The application of the proposed screening criteria is illustrated in a flowchart (Fig. 4). From our data, it is best to order a sinus plain film first, considering the very high sensitivity in detecting both fungal and bacterial sinusitis. If there is a bilateral disease or presence of air-fluid levels, bacterial sinusitis is more likely. If there is total opacification of the unilateral maxillary sinus, sinus ultrasound should be performed at the same time. If the ultrasound is negative, a CT scan should be arranged due to a high suspicion of fungal infection. For patients who do not fulfill the criteria, medication including oral antibiotics can be considered first. If a complete response to medical therapy cannot be achieved, a CT scan is suggested for a survey of etiology.

A small proportion of patients with fungal sinusitis had little or no calcifications in the maxillary sinus and were more likely to have a positive sinus ultrasound. This finding lowers the sensitivity of the screening process and should be kept in mind as a limitation of this method. Other limitations of our study included limited sample size and retrospective nature. In 6 years, we only included 48 patients in this study. Our institution is a tertiary medical center, and a large proportion of patients are referred from local clinics or regional hospitals. Many of them already had a CT scan, especially patients with fungal sinusitis. In this situation, we do not order any other imaging exam. Hence, fewer patients had both preoperative sinus plain films and ultrasound available for analysis. 89.6% of our study subjects had two exams done within two weeks.

This study provides evidence for the remarkable false negative rate of sinus ultrasound in fungal maxillary sinusitis. Physicians should be very cautious while managing patients with negative ultrasound but simultaneously positive sinus plain film. Further prospective studies with a larger sample scale are needed to validate the cost-effectiveness of this method in the future.

In conclusion, a positive sinus plain film combined with a false negative sinus ultrasound, as the diagnostic criteria for fungal maxillary sinusitis, can potentially become an easy and cost-effective screening tool before the diagnostic CT scan.

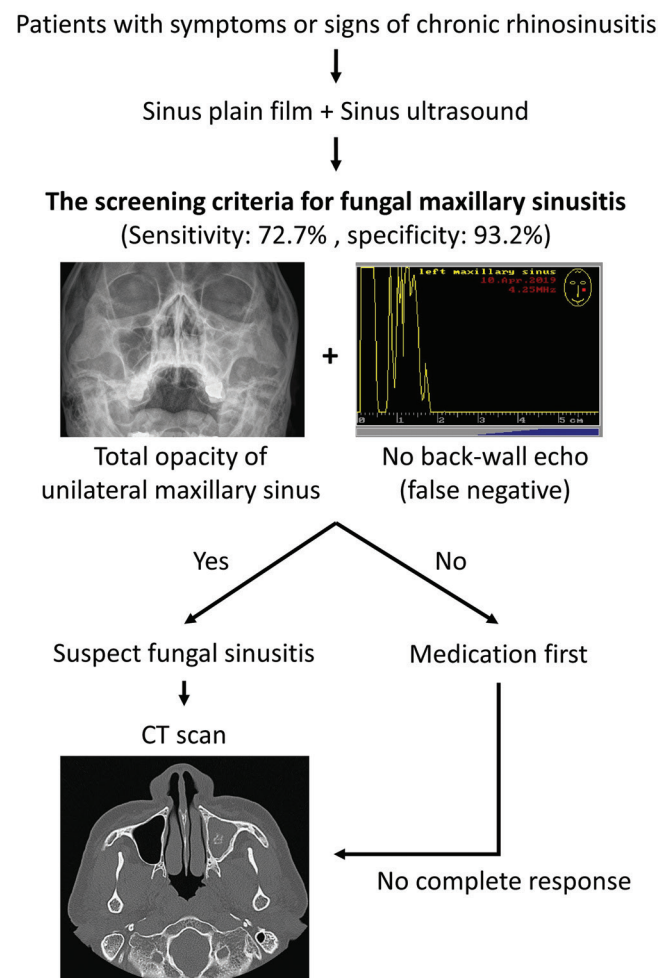


Fig. 4 Flowchart of the proposed screening criteria for fungal maxillary sinusitis. The screening criteria for fungal maxillary sinusitis is defined as the combination of a positive sinus plain film and a false negative sinus ultrasound. CT = computed tomography.

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