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Increased risks of maxillary sinus mucosal thickening in Chinese patients with periapical lesions

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ABSTRACT

Objectives: This study aimed to evaluate the effects of factors related to periapical lesions (PALs) on sinus membrane thickening (SMT) in the Chinese population using cone-beam computed tomography (CBCT).
Methods: In this retrospective study, CBCT images (n = 512) of maxillary sinuses of 446 patients were evaluated by two examiners for SMT and PALs, PAL size, and the distance between the maxillary sinus floor (MSF), and the PAL's edge/root apex. The data were analyzed using analysis of variance, the Kruskal-Wallis test, χ^2-test, and logistic regression.
Results: A binary logistic regression model showed that the prevalence and severity of SMT > 2 mm were significantly associated with older age (>60 years) (odds ratio [OR]: 4.03, 95% confidence interval [CI]): 2.24–7.72, $P < 0.001$], male sex (OR: 2.08, 95% CI: 1.21–3.56, $P < 0.006$), and PALs (OR: 6.89, 95% CI: 3.93–12.08, $P < 0.001$). The type of contact and penetration between the MSF and PALs or root apex showed a more significant relation with SMT > 2 mm than did distance after adjusting for confounding factors, including age and sex (PALs: OR = 10.17 and 14.57, $P < 0.001$; root apex: OR = 3.49 and 5.86, $P < 0.001$).
Conclusions: The prevalence and severity of SMT were significantly associated with older age, male sex, PALs, PAL size, and the distance between the MSF and PALs/root apex. Therefore, communication between dental surgeons and an otolaryngology specialist is important for the timely diagnosis and treatment of SMT of dental origin.

1. Introduction

The maxillary sinus (MS) is a pyramid-shaped cavity in the facial skull. It is the largest paranasal air-filled space and can be divided into five walls [1]. The MS lining is covered by the Schneiderian membrane (SM), a mucous membrane [2]. The SM consists of an overlaid periosteum with a thin layer of pseudo-stratified ciliated epithelium (usually 0.8–1.0 mm thick) and highly vascularized

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connective tissue, which can be difficult to see on imaging [3]. Infection or allergic stimulation can increasethe periosteum's thickness by 10–15 times [4]. Sinus membrane thickening (SMT), the most common MS abnormality, is an inflammatory reaction characterized by hyperplasia of the MS mucosal epithelial cells with a prevalence rate of 38–66% [5,6]. The range in the reported prevalence rates could be due to differences in race, environment, and diagnostic criteria, and the definitions of SMT uesd [7]. However, most researchers accept a mucosal thickness of greater than 2 or 3 mm as pathological SMT [8–10].

Maxillary molars are adjacent to the MS, and odontogenic infection is one of the main causes of maxillary sinusitis. Previous studies have found that odontogenic maxillary sinusitis (OMS) causes approximately 10–51.8% of all maxillary sinusitis cases [9,11]. Rey--Martínez et al. [12] found that among the odontogenic infections, periodontitis (47.1%), apical pathology (23.5%), and endodontic treatments (23.1%) were the predominant causes of SMT cases with a mucosal thickness greater than 2 mm. Although inconclusive, a relationship between periapical lesions (PALs) and the SMT has been suggested. While most studies have reported a positive correlation [13–21], others have found no significant association [6,10,22–24]. A systematic review conducted in 2020 reported a significant association between PALs and SMT (odds ratio [OR] = 2.43)and OMS (OR = 1.77) [25] and showed that the prevalence of SMT was directly related to the PAL size and inversely related to the distance of the lesion/root apex from the maxillary sinus floor (MSF) [15,26–28]. However, other studies found no correlation between SMT and the size of PALs [19] or their distance from the MSF with sinus abnormalities [14,19,21]. Further studies are required to consolidate the relationship between various factors of PALs and SMT.

Digital periapical radiography, panoramic radiography, computed tomography (CT), cone-beam computed tomography (CBCT), lateral cephalometry, and magnetic resonance imaging have been used to diagnose diseases associated with the MS [29–31]. Digital periapical and panoramic radiography fail to precisely determine the sinus anatomy due to limited view fields, superimposition of three-rooted maxillary teeth, and the zygomatic process on the MSF [23,32,33]. The introduction of CBCT in 1998 was an important development in dentomaxillofacial radiology [34], the allowed the precise visualization of the sinus anatomy. Although CT is considered the gold standard method for imaging paranasal sinuses [30], CBCT is preferred due to its higher resolution [35], lower scanning time [14], and exposure to lower doses of radiation [36]. Therefore, we used CBCT to evaluate the MS in the present study.

It is essential to evaluate the condition of the posterior maxillary region before routine dental treatments, including extraction and root canal treatment, especially in patients with apical periodontitis and implants. The role of PALs in the MS in the Chinese population has only been reported in two studies [14,37]. Both studies found that PALs were associated with SMT. However, neither study presented a robust analysis of the periapical index (PAI) well. One article only evaluated whether the participants had PALs, without an evaluation of the PAI PAI scores [37]. Other used an old evaluation criteria of the PAI [14]. The PAI ranges from healthy to severe periodontitis based on the interpretation of 2-dimensional radiographic images [38], whereas the new PAI criteria was established according to the interpretation of 3-dimensional CBCT scans [39]. Compared with the old PAI, the new PAI criteria allows for detection of lesions that are not visible radiographically and produces quantitative values, which can decrease false-negative diagnosis, minimize the interference of researchers, and increase the reliability of clinical studies, especially those referring to the prevalence and severity of PALs [39]. Moreover, whether SMT is related to the distance between the roots/PALs and the MSF is not well understood. Therefore, this study used the new PAI based on CBCT to determine SMT's association with age, sex, periapical status of the upper premolars and molars, size, and distance from the PALs and root apex to the MSF. We hypothesized that an increase in age and PAL size is associated with an increase in SMT.

2. Materials and methods

2.1. Subjects

In this retrospective study, we randomly selected patients with dental problems who were referred to the Department of Radiology in Shanghai Fifth People's Hospital, affiliated with Fudan University. We conducted a pilot study to determine a sufficient sample size for the primary study using relevant statistical methods and literature reports. We searched the hospital database for patients treated between January 2018 and December 2021. CBCT images of 446 patients meeting the inclusion and exclusion criteria were included in the study. Patients with at least one premolar or molar tooth on the left or right side (completely erupted teeth excluding the third molars) were included in the study. We excluded patients (1) under 18 years of age; (2) with maxillary CBCT scans of non-optimal quality for diagnostic purposes; (3) with allergies, cold, or infections of the upper respiratory tract in the last 4 weeks; (4) previously diagnosed with acute or chronic maxillary sinusitis, asthma, osteoporosis, trauma to the integrity of the MS, and neoplasms in the craniofacial region; and (5) with maxillo-mandibular lesions or history of any MS-related surgery.

This study was approved by the Ethics Committee of the Fifth People's Hospital of Shanghai, Fudan University [(2017) 082] and was conducted in full accordance with the World Medical Association Declaration of Helsinki. Due to the retrospective nature of the study, the requirement for informed consent was therefore waived by the Ethics Committee of the Fifth People's Hospital of Shanghai, Fudan University. All data were anonymized.

2.2. Research methods

All images were collected and measured using the ProMax3Ds (Planmeca OY, Helsinki, Finland) imaging system of the Planmeca CBCT using the I-CAT Cone Beam 3D imaging system (Imaging Sciences International, Hatfield, PA, USA). Images were recorded at 90 kVP and 12 mA, using an exposure time of 27 s. Data were collected from 0.2 mm axial, coronal, and sagittal slices through multiplanar reconstructions using the Romexis 3.83 software program (Planmeca OY).

2.3. Assessment of SMT

The MS was diagnosed on a 1:1 scale, using three orthogonal slice views (axial, coronal, and sagittal).

Inflammation of the mucosa causes an increase in, which can be visualized radiographically. Mucosal thickness was measured in millimeters to the nearest 0.01 mm using the coronal and sagittal sections of CBCT scans. Measurements were made at the point of maximum thickness from the MSF to the uppermost point of the thickened mucosa. The data of the two sections were recorded and the average value was taken. The SMT was categorized according to Shanbhag et al. [13] and SMT > 2 mm was considered as pathological sinus membrane inflammation [9]. Fig. 1 shows the CBCT images for the different SMT classes.

Class 0: 0 mm < SMT ≤ 2 mm, normal MS mucosa (in Figure A1 and A2),

Class 1: 2 mm < SMT ≤ 4 mm (in Figure B1 and B2),

Class 2: 4 mm < SMT ≤ 10 mm (in Figure C1 and C2),

Class 3: SMT > 10 mm (in Figure D1 and D2).

Cone-beam computed tomography images showing the classification of SMT on coronal and sagittal views. A1 and A2: Class 0 (normal mucosal thickening, 0 mm < SMT ≤ 2 mm); B1 and B2: Class 1 (2 mm < SMT ≤ 4 mm); C1 and C2: Class 2 (4 mm < SMT ≤ 10 mm); D1 and D2: Class 3 (SMT > 10 mm).

2.4. Assessment of the periapical status

The presence of PALs and their diameters were recorded when (a) the lamina dura was imperceptible or had an irregular appearance and (b) there was radiolucency indicating bone destruction around the root apex. In cases with multiple periapical lesions near the sinuses, only the lesion most closely related to the sinus was recorded.

The following parameters were used to evaluate the CBCT images:

- Tooth type (premolar or molar)
- Root type (buccal, tongue, mesial buccal, distal buccal, or palatine)
- Diameter of PALs
- Distance between PALs and the MSF

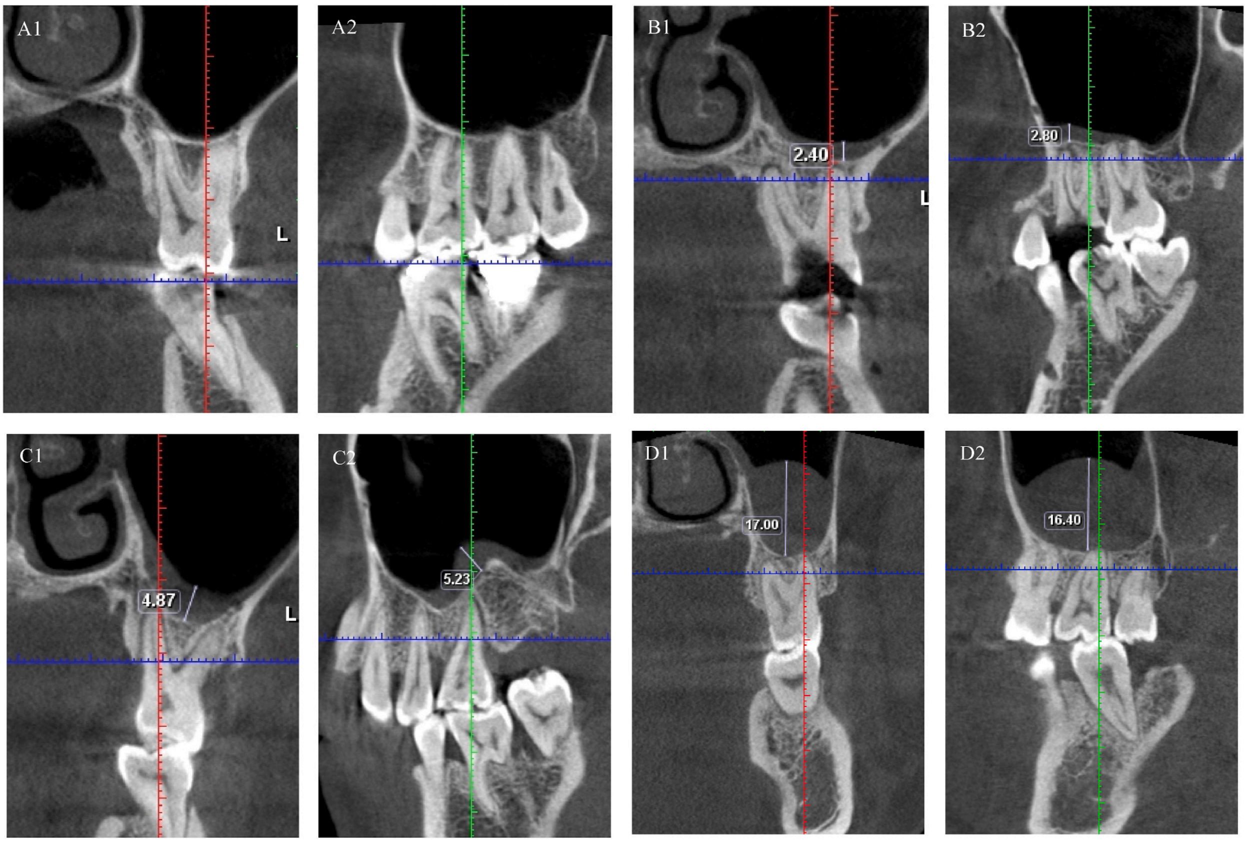

Fig. 1. Classification of maxillary sinus membrane thickening (SMT).

- Distance between the root apex and the MSF

2.4.1. Diameter of PALs

PAL diameters were measured based on the CBCT periapical index (CBCT PAI) developed by Estrela et al. [39] and scored as follows:

Class 0: Intact periapical bone structures.
Class 1: Diameter of periapical radiolucency > 0.5–1 mm,
Class 2: Diameter of periapical radiolucency > 1–2 mm,
Class 3: Diameter of periapical radiolucency > 2–4 mm,
Class 4: Diameter of periapical radiolucency > 4–8 mm,
Class 5: Diameter of periapical radiolucency > 8 mm.

2.4.2. Distance between PALs and the MSF

The closest distance between PALs and the MSF was measured and recorded in the sagittal and coronal views. The distance was classified per the guidelines proposed by Lu et al. [14]. Fig. 2 shows the CBCT images for different anatomic relationships between the MSF and PALs.

Type I: Distance (no contact) between the lesion and MSF (in Figure E),
Type II: Lesion is in contact with the MSF (in Figure F),
Type III: Lesion has penetrated the MSF (in Figure G).

Cone-beam computed tomography images showing the anatomic relationships between maxillary sinuses and PALs. E: Type I, characterized by the distance between the lesion and the MSF; F: Type II, lesion is in contact with the MSF; and G: Type III, lesion has penetrated the MSF.

2.4.3. Distance between the root apex and MSF

The distance of the root apex closest to the MSF was considered for classifying each tooth in the sagittal and coronal views [14]. Fig. 3 shows the CBCT images for the different anatomic relationships between the MSF and root apex.

Type I: Root apex is near (distance > 0 mm) the MSF (in Figure H),
Type II: Root apex is in contact (distance 0 mm) with the MSF (in Figure I),
Type III: Root apex protrudes into the MSF (distance < 0 mm) (in Figure J).

Cone-beam computed tomography images showing the anatomic relationships between maxillary sinuses and the root apex considering the distance between the MSF and root apex. H: Type I, root apex is near the MSF; I: Type II, root apex in contact with the MSF; and J: Type III, root apex protrudes into the MSF.

Two researchers performed the 3D reconstructions and axial, sagittal, coronal planes analyse on the scanned images after being trained by an oral radiologist (with more than 20 years of experience) and passing a standard confirmation test. Each researcher recorded 20 images twice (at an interval of 2 weeks) to assess the intra-examiner reliability. Inter-examiner reliability was measured by having an experienced oral radiologist repeat the measurements for the same 20 images.

2.5. Statistical analysis

Statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY, USA). Patients with any missing data were excluded.

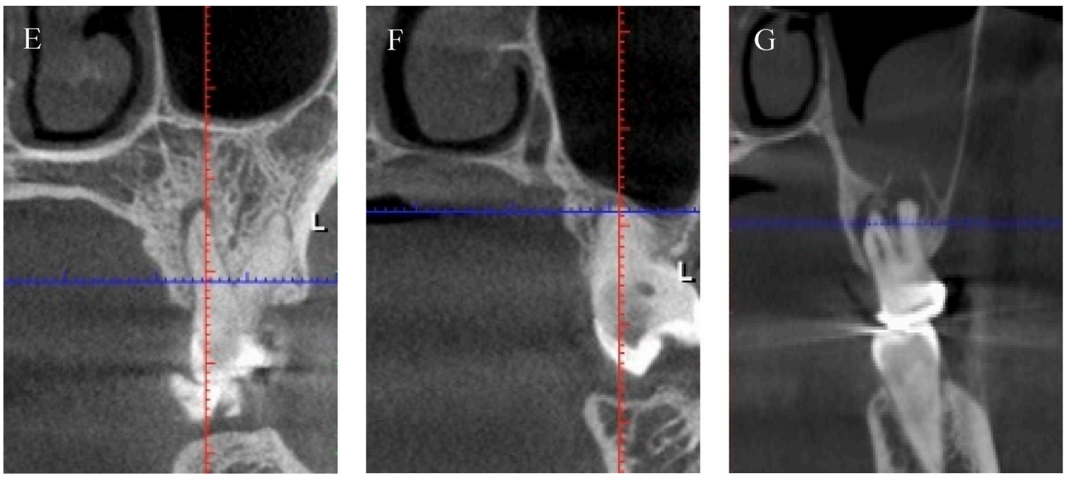

Fig. 2. Distance between the periapical lesions (PALs) and maxillary sinus floor (MSF).

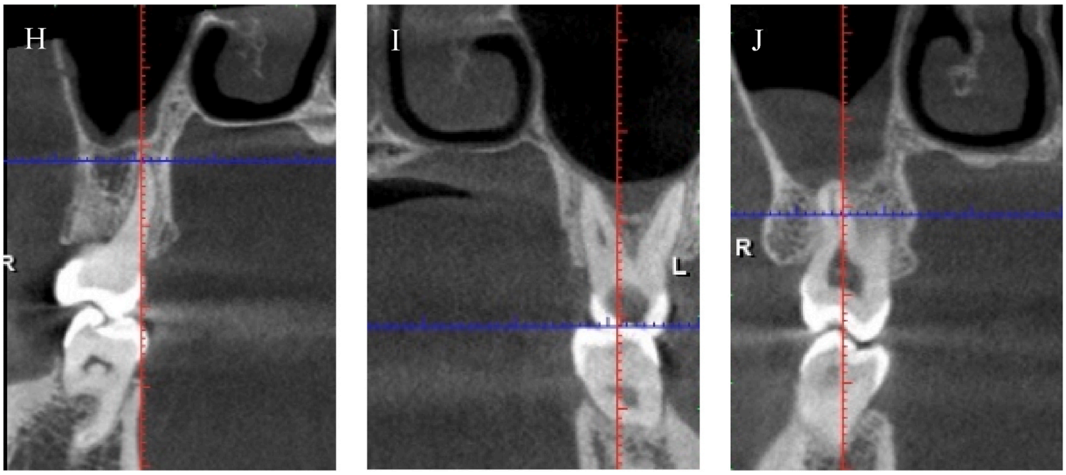

Fig. 3. Distance between the root apex and maxillary sinus floor (MSF).

Continuous variables with or without a normal distribution are presented as the mean ± standard deviation or as median with interquartile range, respectively. Groups were compared using analysis of variance or the Mann-Whitney test (two groups) or the Kruskal-Wallis test (three and more groups) depending on the presence or absence of a normal distribution, respectively. Count data

Table 1
Demographic characteristics of the subjects.

Demographic Variables		
All patients, n		446
Age, years, M (IQR)	42 (29–62)	
Sex, n (%)		
	Male	211 (47.3)
	Female	235 (52.7)
Maxillary sides, n (%)		
	Right	182 (40.8)
	Left	198 (44.4)
	Both right and left	66 (14.8)
All teeth, n		512
Tooth position, n (%)		
	First premolar	19 (3.7)
	Second premolar	38 (7.4)
	First molar	336 (65.6)
	Second molar	119 (23.2)
Root, n (%)		
	Buccal	28 (5.5)
	Tongue	31 (6.1)
	Mesial buccal	142 (27.7)
	Distal buccal	110 (21.5)
	Palatine	201 (39.3)
CBCT PAI, n (%)		
	0	95 (18.6)
	1	41 (8.0)
	2	41 (8.0)
	3	69 (13.5)
	4	181 (35.4)
	5	85 (16.6)
Distance between PAL's edge and the MSF, n (%)		
	I	398 (77.7)
	II	71 (13.9)
	III	43 (8.4)
Distance between the root apex and MSF, n (%)		417
	I	233 (55.9)
	II	105 (25.2)
	III	79 (18.9)

M (IQR): median (interquartile range); CBCT: cone-beam computed tomography; CBCT PAI: CBCT periapical index; PAL: periapical lesion; MSF: maxillary sinus floor.

are reported as percentages or ratios, and intergroup comparisons were conducted using the χ^2 test or the Kruskal-Wallis test. A binary logistic regression analysis was used to determine factors associated with the presence of SMT > 2 mm. The parameters associated with PALs and the SMT were compared among multiple groups using Bonferroni correction. The OR, 95% confidence interval (CI), and *P*-value were calculated. The intra-examiner and inter-examiner reliability were evaluated using the kappa coefficient. $P < 0.05$ indicated statistical significance. Comparisons between three and more groups were made using bonferroni correction. The adjusted-*P* value of the bonferroni correction is $P/[n*(n-1)/2]$, where *P* is the original threshold ($P = 0.05$) and n is the total number of groups.

3. Results

3.1. Study population

The study enrolled 446 patients who underwent CBCT covering 512 MSs. Of these patients, 211 (47.3%) and 235 (52.7%) were men and women. Table 1 summarizes the characteristics of the study participants. SMT was usually unilateral, and the prevalence of SMT > 2 mm was not significantly different in the right and left MSs (54.4% *vs.* 62.1%, $P = 0.145$). A total of 512 teeth were recorded in this study, and 294 (57.4%) of them had SMT > 2 mm, including 204 maxillary first molars (69.4%), 67 maxillary second molars (22.8%), 18 maxillary second premolars (6.1%), and 5 maxillary first premolars (1.7%). In addition, SMT > 2 mm mostly affected the palatal root (43.5%), followed by the mesial buccal root (28.2%) and the distal buccal root (20.4%).

The kappa coefficient of the intra-examiner and inter-examiner agreement were 0.89 and 0.85, respectively ($P < 0.001$), indicating high reliability and satisfactory agreement.

3.2. Prevalence of SMT

As shown in Table 2, age, sex, CBCT PAI, and the distance between the MSF and PAL (upper edge)/root apex were identified as significant factors associated with SMT > 2 mm ($P < 0.05$). The prevalence of SMT > 2 mm increased significantly with age (34.2%, 58.8%, 58.9%, and 73.4% for the age groups 19–25, 26–40, 42–60, and >60 years, respectively, $P < 0.001$). It was also significantly higher in men (65.8%) than in women (49.8%) ($P < 0.001$). Of all the PALs evaluated, 181 (35.4%) were CBCT PAI 4. Bone destruction and/or expansion were seen in 81.4% of the cases with PALs. The prevalence of SMT > 2 mm was significantly higher in patients with the PALs than in those without it (65.9% *vs.* 20.0%, $P < 0.001$). Considering the distance from the PAL's upper edge to the MSF, the incidence of types I and II lesions was significantly higher than that of type III in patients with SMT > 2 mm (78.9% and 83.7% *vs.* 50.8%, $P < 0.001$). Similarly, considering the distance between the root apex and MSF, the prevalence of types I and II lesions was significantly higher than that of type III in patients with SMT > 2 mm (90.5% and 92.4% *vs.* 45.9%, $P < 0.001$).

Table 2
Prevalence of SMT in the study groups.

		0 mm < SMT ≤ 2 mm	2 mm < SMT ≤ 4 mm	4 mm < SMT ≤ 10 mm	SMT > 10 mm	Chi-square	P^a
Age group (years)						58.426	<0.001
n (%)	19–25	63 (34.8)	12 (28.6)	18 (12.9)	7 (8.4)		
	26–40	42 (23.2)	15 (35.7)	42 (30.0)	14 (16.9)		
	42–60	44 (24.3)	8 (19.0)	35 (25.0)	20 (24.1)		
	>60	32 (17.7)	7 (16.7)	45 (32.1)	42 (50.6)		
Sex, n (%)						17.317	0.002
	Male	68 (37.6)	19 (45.2)	73 (52.1)	51 (61.4)		
	Female	113 (62.4)	23 (54.8)	67 (47.9)	32 (38.6)		
CBCT PAI, n (%)							<0.001
	0	76 (34.9)	8 (16.0)	7 (4.5)	4 (4.5)		
	1	23 (10.6)	9 (18.0)	7 (4.5)	2 (2.3)		
	2	18 (8.3)	12 (24.0)	10 (6.4)	1 (1.1)		
	3	25 (11.5)	14 (28.0)	24 (15.4)	6 (6.8)		
	4	55 (25.2)	5 (10.0)	86 (55.1)	35 (39.8)		
	5	21 (9.6)	2 (4.0)	22 (14.1)	40 (45.5)		
Distance between						126.047	<0.001
PAL's edge and	I	126 (88.8)	27 (64.3)	55 (36.9)	25 (29.8)		
the MSF, n (%)	II	10 (7.0)	12 (28.6)	60 (40.3)	23 (27.4)		
	III	6 (4.2)	3 (7.1)	34 (22.8)	36 (42.9)		
Distance between						48.339	<0.001
the root apex	I	196 (89.9)	44 (88.0)	105 (67.3)	53 (60.2)		
and MSF, n (%)	II	15 (6.9)	3 (6.0)	33 (21.2)	20 (22.7)		
	III	7 (3.2)	3 (6.0)	18 (11.5)	15 (17.0)		

SMT: sinus membrane thickening; CBCT: cone-beam computed tomography; CBCT PAI: CBCT periapical index; PAL: periapical lesion; MSF: maxillary sinus floor.
The χ^2-test: $P^a < 0.05$. Comparisons between three and more groups were made using the bonferroni correction. The adjusted-*P* value of the bonferroni correction is $P/[n*(n-1)/2]$, where *P* is the original threshold ($P = 0.05$) and n is the total number of tests.

3.3. Association between SMT and PALs

The median maxillary SMT was 4.62 (1.72–8.71) and 0.80 (0.50–1.75) mm in patients with and without PALs, respectively ($P < 0.001$). In patients with SMT > 2 mm, the median mucosal thickening was 7.17 (4.45–10.28) mm. As shown in Table 3, SMT was significantly higher in older male patients with PALs of types II and III (considering the distance from the PAL to the MSF) ($P < 0.001$).

3.4. Binary logistic regression analysis of PALs and SMT

The binary logistic regression analysis indicated that older age, male sex, PAL sizes, and types II and III (considering the distance between the PAL's upper edge/root apex and MSF) were positively associated with SMT > 2 mm. The ORs and 95% CIs for these associations are shown in Tables 4–6.

The risk of SMT > 2 mm was significantly associated with male sex (OR = 1.76, $P = 0.006$) and older age (OR = 4.03 for age >60 years, $P < 0.001$) (Table 4). The chances of developing SMT > 2 mm further increased in patients with PALs (OR [95% CI]) = 6.89 (3.93–12.08), $P < 0.001$] when compared with those in patients without them.

Patients with PALs that are in contact with the MSF (type II) and have penetrated the MSF (type III) are at a higher risk (10.17 and 14.57 times, respectively) of developing SMT > 2 mm than those with PALs near the MSF (type I) (Table 5).

After adjusting for confounding factors (age and sex), patients with the root apex in contact with the MSF (type II) or protruding into the MSF (type III) were at a higher risk (3.49 and 5.86 times, respectively) of developing SMT > 2 mm than those with the root apex near the MSF (type I) (Table 6).

4. Discussion

This study evaluated the effects of various factors associated with PALs and SMT using CBCT images. The prevalence of SMT greater than 2 mm in patients with PALs was 65.9%. The OR for SMT greater than 2 mm in patients with PALs was 6.89. Moreover, the prevalence and severity of SMT increased with the size of PALs, which are consistent with previous studies [6,37,40,41]. A SMT greater than 2 mm was associated with CBCT PAI (1–5), with ORs of 3.45, 5.44, 6.50, 7.64, and 9.55, respectively. Curi et al. [42] have reported that the presence of PALs increases the chances of SMT by 23.3 times. A recent meta-analysis indicated an OR of 2.43 times in the risk of SMT in patients with PALs [25]. However, other studies have found no significant association between PALs and SMT [6,10,22–24]. This discrepancy is possibly because of the different thresholds used for defining pathological SMT [14,26,27,43], inclusion and exclusion criteria, and different tomographic resolutions or methods for detecting MS [17,24] in each study. While most studies define SMT as a thickness greater than 2 mm [20,21,27,37,41,43] some consider a thickness greater than 1 mm as pathological SMT [4,14,18,19,26]. This could lead to an over- or underestimation of the actual prevalence of SMT. The normal thickness of the MS mucosa,

Table 3
Descriptive values of SMT and PALs.

		SMT (mm)	Average rank	H	*P*
Age group (years)				54.783	<0.001[b]
M (IQR)	19–25 (A)	1.47 (0.80–3.05)	186.32		
	26–40 (B)	3.50 (1.50–5.31)	249.41		B vs A
	42–60 (C)	3.80 (1.38–8.86)	260.7		C vs A
	>60 (D)	6.80 (1.89–10.37)	315.3		D vs A/D vs B/D vs C
Sex, M (IQR)				17.126	<0.001[c]
	Male	4.56 (1.60–9.01)	283.34		
	Female	2.26 (1.17–6.93)	232.26		
CBCT PAI				109.782	<0.001[b]
M (IQR)	0	0.80 (0.50–1.75)	153.36		
	1	1.96 (1.30–3.22)	196.89		1 vs 0
	2	2.43 (1.32–4.39)	215.28		2 vs 0
	3	3.81 (1.40–5.74)	250.34		3 vs 0
	4	6.04 (1.83–9.03)	295.23		4 vs 0/4 vs 1/4 vs 2/4 vs 3
	5	9.26 (2.72–13.89)	342.94		5 vs 0/5 vs 1/5 vs 2/5 vs 3
Distance between				105.263	<0.001[b]
PAL's edge and	I	1.90 (1.30–6.48)	159.04		
the MSF, n (%)	II	6.46 (4.30–9.50)	255.75		II vs I
	III	8.37 (5.90–11.63)	294.22		III vs I
Distance between				44.289	<0.001[b]
the root apex	I	2.20 (1.20–7.04)	234.65		
and MSF, n (%)	II	5.67 (4.05–10.29)	326.44		II vs I
	III	6.93 (4.31–10.58)	343.29		III vs I

M (IQR): median (interquartile range); SMT: sinus membrane thickening; CBCT: cone-beam computed tomography; CBCT PAI: CBCT periapical index; PAL: periapical lesion; MSF: maxillary sinus floor.
[b] the Kruskal-Wallis test: $P < 0.05$. [c] the Mann-Whitney: $P < 0.05$. And comparisons between three and more groups were made using the bonferroni correction. The adjusted-*P* value of the bonferroni correction is $P/[n*(n-1)/2]$, where *P* is the original threshold ($P = 0.05$) and n is the total number of groups.

Table 4
Binary logistic regression analysis of SMT and CBCT PAI.

		SMT > 2 mm	
		OR (95% CI)^d	
Age group (years)			
	19–25	1	
	26–40	2.18 (1.24–3.84)	0.007
	42–60	2.33 (1.31–4.13)	0.004
	>60	4.03 (2.24–7.27)	<0.001
Sex			
	Male	1.76 (1.18–2.63)	0.006
	Female	1	
CBCT PAI			
	0	1	
	1	3.54 (1.55–8.10)	0.003
	2	5.44 (2.38–12.41)	<0.001
	3	6.50 (3.14–13.46)	<0.001
	4	7.64 (4.14–14.11)	<0.001
	5	9.55 (4.62–19.74)	<0.001

SMT: sinus membrane thickening; OR (95% CI): odds ratio (95% confidence interval); CBCT: cone-beam computed tomography; CBCT PAI: CBCT periapical index; PAL: periapical lesion; MSF: maxillary sinus floor.
The binary logistic regression analysis: $P^d < 0.05$.

Table 5
Binary logistic regression analysis of SMT and the distance between PALs and MSF.

		SMT > 2 mm	
		OR (95% CI)	P^e
Age group (years)			
	19–25	1	
	26–40	2.19 (1.09–4.38)	0.027
	42–60	2.31 (1.15–4.66)	0.019
	>60	3.42 (1.71–6.82)	0.001
Sex			
	Male	1.47 (0.91–2.36)	0.117
	Female	1	
Distance between the PAL's upper edge and the MSF	I	1	
	II	10.17 (5.00–20.69)	<0.001
	III	14.57 (6.00–35.39)	<0.001

SMT: sinus membrane thickening; OR (95% CI): odds ratio (95% confidence interval); PAL: periapical lesion; MSF: maxillary sinus floor.
The binary logistic regression analysis: $P^e < 0.05$.

Table 6
Binary logistic regression analysis of SMT and distance between the root apex and MSF.

		SMT > 2 mm	
		OR (95% CI)	P^f
Age group (years)			
	19–25	1	
	26–40	2.74 (1.58–4.76)	<0.001
	42–60	3.26 (1.86–5.69)	<0.001
	>60	5.48 (3.12–9.64)	<0.001
Sex			
	Male	1.88 (1.28–2.77)	0.001
	Female	1	
Distance between the root apex and MSF	I	1	
	II	3.49 (1.85–6.59)	<0.001
	III	5.86 (2.42–14.19)	<0.001

SMT: sinus membrane thickening; OR (95% CI): odds ratio (95% confidence interval); M (IQR): median (interquartile range); CBCT: cone-beam computed tomography CBCT PAI: CBCT periapical index; PAL: periapical lesion; MSF: maxillary sinus floor.
The binary logistic regression analysis: $P^f < 0.05$.

also known as the Schneiderian membrane, is reported to be 0.8–1 mm. Most authors accept greater than 2–3 mm is widely considered as pathological mucosal thickening. Therefore, we considered a sinus mucosa thickness greater than 2 mm as pathological SMT for comparison to previous studies.

Most studies have pointed out that the unilateral onset of SMT is a feature of OMS, in contrast to nasal maxillary sinusitis [44–46]. We also found that SMT was usually unilateral, and the prevalence of SMT greater than 2 mm was comparable in patients with right and left MS ($P = 0.145$). Consistent with other studies [9,13,47], we found that SMT greater than 2 mm mainly affects the maxillary first molars and palatal roots. It has been hypothesized that the first molars are more prone to caries, pulp disease, and PALs than other teeth, resulting in MS lesions. Bacterial products of periapical inflammation, such as lysosomal enzymes, collagenase, and toxins, increase the permeability of the soft tissue, promoting the spread of infection to the MS through the apical foramen to the alveolar bone. These events result in local mucosal edema, hyperplasia, and bone destruction in the MS. Leaving the odontogenic infection untreated can lead to serious complications and pose a significant threat to health [48,49]. Therefore, stomatologists consider the possibility of OMS in the presence of PALs in the maxillary posterior region. The changes in the MS should be closely monitored to prevent and manage lesions in areas adjacent to the MS and OMS.

Our findings show a greater risk/prevalence of SMT > 2 mm and more severe SMT in the older (26–40 years: OR = 2.18; 42–60 years: OR = 2.33; and >60 years: OR = 4.03) and male (OR = 1.76) patients, which are consistent with previous reports [13,14,37]. The older the age, the higher the risk of dental damage; thus, OMS may be detected in older age, increasing the rate of mucosal thickening. In contrast, other studies found no significant difference in the incidence of SMT per sex [28,50] and age groups [1,17,50, 51]. This discrepancy can be explained by the differences in races, regions of the research objects, eating habits, and other confounders.

The distance between the upper edge of the PALs and MSF may be a factor associated with SMT. We found that when the PALs were in contact with the MSF (type II) or penetrate the MSF (type III), the chances of developing SMT > 2 mm were 10.17 and 14.57 times higher than when the PALs are just close to the MSF (no contact, type I). These findings are in line with those of Kuligowski et al. [43], Sghaireen [50], and Dagassan-Berndt et al. [15]. However, Zadsirjan et al. [19], Gürhan et al. [21], Rege et al. [6], and Lu et al. [14] have demonstrated that the proximity between PALs and the MSF has no association with SMT. In general, infection and host resistance may affect the transmission of periapical infection to the MS. Thus, the results should be interpreted with caution, and future studies should consider exploring the relationship between SMT and the proximity between PALs and MSF.

A few studies have evaluated the relationship between SMT and the distance between the root apex and MSF [6,14,52]. We investigated 512 MSs and found that in 77% of the patients, there was some space between the root apex and MSF, while in 8.4%, there was an overlap. In 13.9% of the patients, the root apex touched the MSF, which was consistent with the findings of Oberli et al. [52]. Two studies reported no relationship between SMT and the proximity between the root apex and MSF [6,14]. Contrastingly, we found a significant relationship between the prevalence of SMT > 2 mm and the proximity between the diseased roots and MSF. Furthermore, patients with the root apex in contact with the MSF (type II) and those that protruded into the MSF (type III) were at greater risk (3.49 and 5.86 times, respectively) of developing SMT > 2 mm than those with the root apex near the MSF (type I), after adjusting for confounding factors (age and sex). Oliveira de Lima et al. [53] found a 2.5-fold lower risk of OMS when the tooth with the endodontic infection was located further from the sinus, which is consistent with our findings. We believe that increased incidence and severity of SMT are related to the decrease in the bone thickness between the lesions and the MSF and the weakened barrier effect of metabolites. Pathological bacteria, toxins, and proinflammatory cytokines from the proximity of periapical lesions may directly infiltrate the MS through the thin and porous maxillary bone, numerous blood, and lymphatic vessels [43]. Therefore, the tooth that presents with a PAL closer to the MSF is more likely to propagate microorganisms to the MS. Hence, when the root of the maxillary posterior teeth overlaps or touches the MSF, attention should be paid to the occurrence of OMS. Moreover, exogenous infections entering the MS should be prevented during the treatment of affected teeth.

This study had some limitations. First, as this study was a cross-sectional retrospective study, our findings cannot explore the temporal relationship. The findings do not explain causal relationships between factors associated with PALs and SMT. Second, participants were recruited from one hospital which limits the generalizability and increases the chance of selection bias. Third, data were not available for smoking status, occupation, and dietary habits of the study subjects, which may have influenced the study outcomes. Therefore, well-designed, prospective, longitudinal studies of patients with and without PALs and SMT are needed to clarify f the relationship between PALs and SMT and their common mechanism of pathogenesis. Moreover, clinical studies must determine whether treating PALs reduces or cures SMT.

5. Conclusions

The OMS has a higher prevalence in older men among the population that visit dentists. The risk of SMT > 2 mm increases with the presence of PALs in the maxillary posterior teeth, especially as the lesions increase in size and the lesion and root apex get closer to the MSF. Therefore, patients with PALs in the maxillary posterior area should be monitored for OMS and other sinus symptoms. If OMS is suspected, a detailed examination should be conducted as soon as possible to make a clear diagnosis, and a comprehensive treatment plan should be formulated in the early stages in consultation with otorhinolaryngology specialists.

Ethics approval and consent to participate

This study was approved by the Ethics Committee of the Fifth People's Hospital of Shanghai, Fudan University [(2017) 082] and was conducted in full accordance with the World Medical Association Declaration of Helsinki. The privacy rights of human subjects must always be observed. All procedures were performed in accordance with relevant guidelines. The data are anonymous, and the requirement for informed consent was therefore waived by the Ethics Committee of the Fifth People's Hospital of Shanghai, Fudan University.

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Author contribution statement

Limin Zhang, Yanan Zhang, Yinghua Li and Liang Song: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Qimei Xu, Jingjing Shu and Yue Hu: Performed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper. Bin Xu, Liuhui Liu and Huijuan Chen: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability

The data and code used for the analysis were available from the corresponding authors upon request.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Abbreviations

PALs	periapical lesions
SMT	sinus membrane thickening
MSF	maxillary sinus floor
OR	odds ratio
CI	confidence interval
MS	maxillary sinus
SM	Schneiderian membrane
OMS	odontogenic maxillary sinusitis
CT	computed tomography
CBCT	cone-beam computed tomography
M (IQR)	median [interquartile range]

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