

Characteristics and risk factors of mucosal cysts in the paranasal sinuses*

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SUMMARY

Background: Though mucosal cysts in the paranasal sinuses (PSMCs) are common findings on radiographic images, the nature of PSMCs and risk factors for the development of PSMCs have not yet been determined. The aim of this study was to evaluate the characteristics of PSMCs using brain magnetic resonance (MR) imaging.

Methodology/Principal: A total of 6831 subjects who underwent health checkup including brain MR imaging were included in this study. The characteristics of PSMCs, including their location, number and size, as well as the presence of obstruction of the sinus ostium and sinusitis, were analysed using brain MR images. Structured questionnaires and medical records were reviewed to evaluate the smoking status and comorbid medical conditions.

Results: The overall prevalence of PSMCs was 7.4% and was significantly higher in females than in males. PSMCs were most commonly found in the maxillary sinus, most of which were located unilaterally as a solitary cyst. Large cysts were associated with obstruction of the sinus ostium and subsequent sinusitis. Smoking was a single important risk factor for developing PSMCs. No significant associations were found between symptoms (nasal/respiratory) and the presence of PSMCs.

Conclusions: The prevalence of PSMCs was 7.4% and decreased with age. Large cysts may lead to obstruction of the sinus and subsequent sinusitis. Smoking was an important risk factor for PSMCs, and the total amount of smoking correlated with cyst size. Most subjects were asymptomatic, and specific treatment was not performed.

Key words: paranasal sinuses, cysts, magnetic resonance imaging, age factors, smoking, risk factors

INTRODUCTION

Dome-shaped or cyst-like radiopaque lesions are commonly observed on the wall of the paranasal sinuses on simple radiographs, including Waters' and panoramic views, computed tomography (CT) and magnetic resonance (MR) imaging of the paranasal sinuses and brain. They are usually asymptomatic and found on routine radiographic examination taken for other reasons. They are well recognized as mucosal cysts arising from the wall of the paranasal sinuses (PSMCs), and their reported prevalence in the general population varies from 3.2% to 35.6%⁽¹⁻⁴⁾. Recently, imaging technologies have been dramatically improved, and more sensitive techniques such as CT or MRI have become widely used, which result in an increase in their prevalence.

The clinical implications of PSMCs remain uncertain. PSMCs have generally been accepted as benign, but there is debate as to whether they are an entirely benign and ignorable finding or a kind of sinus pathology. In addition, the risk factors for the development of PSMCs still remain unclear. Some authors have reported an association between PSMCs and various clinical symptoms, such as headache, nasal obstruction, facial pain and rhinorrhea⁽⁵⁻⁶⁾. Moreover, it has been reported that chronic sinusitis plays an important role in the development of PSMCs^(4,7). However, many patients are asymptomatic in a clinical setting, and a recent study suggests that the occurrence of PSMCs is not associated with sinus or dental diseases and do not require surgical resection.

The size of PSMCs varies according to their location, and it may be possible that the sinus outflow tract is more frequently obstructed with increasing size. However, the correlations between the size of PSMCs and the patency of the sinus outflow tract/subsequent sinusitis have not yet been investigated in a large population study. There have been few reports regarding the associations between other medical conditions, such as allergic rhinitis, and the development of PSMCs. Moreover, the link between smoking, known as an important risk factor for many other sinus diseases, and PSMCs has not yet been examined.

Since PSMCs are commonly found on radiographs, it is necessary to identify the characteristics of PSMCs and to evaluate the risk factors for the development of PSMCs. However, previous studies were limited by a small sample size, and studies with a large population have not yet been conducted. Therefore, we evaluated a large series of brain MR images to determine the current prevalence and nature of PSMCs and to investigate the risk factors for their development.

MATERIALS AND METHODS

Patients

This retrospective study reviewed the records of the subjects who consecutively underwent health checkup including brain MRI at the Healthcare Gangnam Center of Seoul National University Hospital between January 2008 and December 2009. A total of 6,831 subjects were included in this study. There were 2,793 male subjects (40.9%) and 4,038 female subjects (59.1%), and the mean age of the subjects was 53.47 ± 10.55 years (range, 11 - 95 years).

MRI

All subjects underwent brain MRI (Intera Achieva 1.5T, Philips Medical Systems, Best, the Netherlands) as part of the routine medical checkup. The MR images obtained were reviewed using a picture archiving and communications system (Maroview, Marotech, Seoul, Korea) by 2 experienced otorhinolaryngologists (I.J.M. and S.T.K.). PSMCs were radiologically diagnosed by using the following criteria: 1) homogenous dome-shaped cysts with sharp demarcation of the lateral border; 2) absence of bone destruction; 3) absence of communication with tooth roots (to exclude odontogenic cysts); and 4) a smooth, spherical outline along the free border of the cysts^(1,3). Lesions with diffuse mucosal thickening or other irregular opacification were excluded. The characteristics of PSMCs, such as location, number and size, were analyzed. The greatest dimension of PSMCs was measured on sagittal, axial and coronal images. When multiple cysts were present, the location and size of the largest one was used in our analysis. For each subject, the patency of the sinus outflow tract was assessed. If there were discrepancies between the 2 examiners, the discrepancies were resolved by consensus.

Questionnaire

The smoking data was collected using a structured smoking

questionnaire. This questionnaire specifically included questions about a history of smoking in terms of packs per day, number of years smoked, starting age of smoking and duration of smoking cessation. One pack-year smoking was defined as having smoked one pack or 20 cigarettes per day for 1 year. In addition, comorbid medical conditions, such as hypertension, diabetes mellitus, gastric ulcer, asthma and allergic rhinitis, were identified by using both a structured comorbidity questionnaire and medical records. Additionally, nasal symptoms (nasal obstruction, sneezing and rhinorrhea) and upper airway symptoms (postnasal drip, wheezing, cough and sputum) during the 1 month prior to MR imaging were evaluated in all subjects using a questionnaire.

The prevalence of PSMCs in our consecutive series of MR imaging was calculated for all subjects as well as for sex- and age-specific groups. An analysis was performed to identify the relationship of age and sex to the presence of PSMCs and cyst size.

Statistics

Statistical analyses were conducted by using Statistical Package for Social Sciences system, version 12.0 (SPSS Inc, Chicago, IL, USA). Univariate analyses including the *t* test and the Pearson's Chi-square test were used to compare data between the groups with and without PSMCs. Additionally, the effect of various risk factors on the development of PSMCs was evaluated by multivariate analysis. A *p* value of < 0.05 was considered statistically significant. Tophe Institutional Review Board of our hospital approved the study protocol.

RESULTS

Of the 6831 subjects, 501 (7.4%) had PSMCs. The prevalence and size of PSMCs according to distribution, laterality, number and total smoking amount are summarized in Table 1.

PSMCs were most commonly found in the maxillary sinus (477/501, 92.7%), followed by the sphenoid (26/501, 5.0%), frontal (9/501, 1.7%) and ethmoid (3/501, 0.6%) sinuses (Table 1). In addition, PSMCs were most commonly located in the inferior wall within the sinus (297, 59.3%) followed by posterior (63, 12.6%), anterior (59, 11.8%), medial (38, 7.6%), lateral (24, 4.8%) and superior (20, 4.0%) walls (data not shown).

Unilateral cysts were found in 411 (82.0%) of 501 subjects, and bilateral cysts in 90 (18.0%) subjects. PSMCs were larger in the bilateral group than in the unilateral group ($p = 0.000$). Solitary cysts were found in 377 (75.2%) of 501 subjects, and multiple cysts in 124 (24.8%) subjects. There was no significant difference in cyst size between the 2 groups.

The mean age of the subjects with PSMCs was 51.3 years, with a female to male ratio of 3.04:1. The prevalence and size of PSMCs according to sex and age are shown in Table 2. The prevalence of PSMCs was higher in female subjects ($n = 377/3661$; 9.3%) than in male subjects ($n = 124/2,669$; 4.4%; $p = 0.000$). The prevalence of PSMCs significantly tended to

Table 1. Prevalence and size of PSMCs according to distribution, laterality, number and total smoking amount.

	Prevalence	Cyst size (mm)
Distribution of PSMCs in the sinuses		
Maxillary sinus	477/515* (92.7%)	16.79 ± 7.19 [†]
Sphenoid sinus	26/515* (5.0%)	11.61 ± 3.66 [†]
Frontal sinus	9/515* (1.7%)	11.24 ± 6.21 [†]
Ethmoid sinus	3/515* (0.6%)	11.39 ± 2.07 [†]
Laterality		
Unilateral	411/501 (82.0%)	16.34 ± 7.11 [‡]
Bilateral	90/501 (18.0%)	19.90 ± 8.05 [‡]
Number of cysts		
Single	377/501 (75.2%)	17.09 ± 7.48
Multiple	124/501 (24.8%)	16.64 ± 7.21
Total smoking amount		
Never smoker	250/501 (49.9%)	16.41 ± 7.02 [§]
≤ 20 pack-year	138/501 (27.5%)	16.60 ± 6.70 [§]
> 20 pack-year	113/501 (22.6%)	18.71 ± 8.75 [§]

*Numbers are not mutually exclusive.

The size of the largest cyst was used when multiple cysts were present

[†] p = 0.000 by the ANOVA test

[‡] p = 0.000 by the independent t-test

[§] p = 0.018 by the ANOVA test

Table 2. The prevalence and size of PSMCs according to age.

Age (yr)	No. of subjects	Male	Female	Overall prevalence*	Prevalence in males	Prevalence in females	Cyst size [†] (mm)
<29	150	76	74	16 (10.7%)	7 (9.2%)	9 (12.2%)	16.36±6.38
30-39	504	226	278	43 (8.5%)	10 (4.4%)	33 (11.9%)	15.46±6.60
40-49	2023	744	1,279	178 (8.8%)	29 (3.9%)	149 (11.6%)	17.70±8.03
50-59	2476	1030	1446	175 (7.1%)	47 (4.6%)	128 (8.9%)	17.24±7.32
60-69	1321	580	741	74 (5.6%)	28 (4.8%)	46 (6.2%)	16.01±6.95
70-	357	137	220	15 (4.2%)	3 (2.2%)	12 (5.5%)	15.18±5.33
Total	6831	2793	4038	501 (7.3%)	124 (4.4%) [‡]	377 (9.3%) [‡]	16.98±7.41

* p = 0.000 by linear association.

[†] p = 0.307 by the ANOVA test

[‡] p = 0.000 by the Pearson's Chi-square test

decrease with age (p = 0.000). However, there was no significant correlation between age and cyst size (p = 0.307).

The association between cyst size and the presence of sinusitis/obstruction of the sinus ostium by PSMCs is shown in Figure 1. The mean cyst size in subjects with sinusitis was significantly larger than that in those without sinusitis (22.40 ± 8.51 mm vs. 16.41 ± 7.05 mm, p = 0.000). In addition, the mean cyst size in subjects with the sinus ostium being obstructed by the cysts was significantly larger than the size in those without (24.14 ± 9.48 mm vs. 15.93 ± 6.43 mm, p = 0.000). The relationship between the obstruction of the sinus ostium and the presence of sinusitis is presented in Table 3. For subjects with the sinus ostium being obstructed by PSMCs, the odds ratio of the risk for the development of sinusitis was 23.209 (95% confidence interval, 11.646 - 46.249).

To assess whether smoking and other comorbid medical conditions were related to the risk of PSMCs, we examined the relative risk of PSMCs associated with smoking status and comorbid medical conditions at diagnosis. By univariate

analyses including the independent *t* test and the Pearson's Chi-square test to compare data between the groups with and without PSMCs, allergic rhinitis and smoking status had a significant influence on the development of PSMCs. Other comorbid medical conditions including hypertension, diabetes mellitus, gastric ulcer and asthma did not show a significant relationship with PSMCs (data not shown). Therefore, the multivariate model included allergic rhinitis and smoking status (Table 4). By multivariate analysis, smoking status was the only risk factor for the development of PSMCs. When subjects who never smoked were considered as the reference group, there was an elevated risk (RR, 1.939; 95% CI, 1.531-2.456) for PSMCs associated with current smoking. Additionally, the size of PSMCs correlated with total smoking amount (Figure 2) and a history of more than 20 pack-year smoking was associated with an increase in the size of PSMCs (Table 1).

There were no significant associations between nasal symptoms (nasal obstruction, sneezing and rhinorrhea) upper airway symptoms (postnasal drip, wheezing, cough and sputum) and the presence of PSMCs. Only 13 (2.6%) of the 501 subjects

Table 3. Association between the obstruction of the sinus ostium by PSMCs and the subsequent development of sinusitis.

	Obstruction of the sinus ostium by PSMCs		Total
	Absence	Presence	
No sinusitis	420	33	453
Sinusitis	17	31	48
Total	437	64	501

$p = 0.000$ by the Pearson's Chi-square test

Odds ratio = 23.209 (95% confidence interval, 11.646 - 46.249)

Odds ratio was calculated as the risk of sinusitis in subjects with obstruction of the sinus ostium as compared to that in those without.

complained of nasal symptoms. Upper airway symptoms were present in only 8 (1.6%) of 501 subjects with PSMCs.

DISCUSSION

Although the nature of PSMCs is not well defined, these cysts are usually considered to be an incidental finding in imaging studies of the paranasal sinuses. The prevalence of PSMCs has been reported in a relatively small number of subjects^(1,3). MRI is found to be better than CT for evaluating soft tissue lesion such as PSMCs⁽⁸⁾. Therefore, we used a large cohort of healthy individuals who underwent MR imaging for routine medical checkups to evaluate the characteristics and risk factors for PSMCs. PSMCs were found in 501 (7.33%) of the 6,831 brain MR imaging studies. This result is in agreement with those of previous studies, which were between 3.2% and 9.6%^(2-3,5). PSMCs were most commonly located in the maxillary sinus, and rarely located in the frontal or ethmoid sinuses. There was a female predilection in our study, which is in contrast to those found by other investigators^(2,4,9). However, the small sample sizes in previous studies make their results speculative. Although the reason for the difference between the results of previous studies and ours is not clear, the difference may be attributed to the sample size.

The pathogenesis of PSMCs remains unclear. It is postulated that PSMCs are formed when the duct of a seromucinous gland in the paranasal sinus is blocked by inspissated mucus or damaged during an inflammatory episode. The obstructed duct becomes dilated, which forms an epithelium-lined true cystic structure⁽¹⁰⁾. The maxillary sinus is the biggest one among the 4 paranasal sinuses, and this may possibly explain the high incidence of mucosal retention cysts in the maxillary

sinus. Further studies with a prospective design are needed to confirm our results.

Our study revealed a significant relationship between a decrease in the prevalence of PSMCs and an increase in age. Based on this result, it is conceivable that PSMCs are benign and tend to disappear with time. However, this result is inconsistent with that of a previous study demonstrating no association between cyst size and the patient's age⁽¹¹⁾. There are some explanations for this difference. First, diagnosis was made with plain radiographs in the previous study, which could not detect very small PSMCs. Second, racial difference between the previous study and ours might account for the different results. Despite decreasing prevalence with age, we noted that the cysts were of similar size regardless of age groups. Further longitudinal studies with a large population are needed to confirm our results and to determine the natural course of PSMCs.

PSMCs were located unilaterally in most patients. Cyst size was larger in subjects with bilateral PSMCs than in those with unilateral PSMCs. The subjects with large cysts may have a high risk for developing bilateral PSMCs. Multiple cysts were found in approximately 25% of all subjects. In our study, large cyst size was significantly associated with obstruction of the sinus ostium. The risk of sinusitis was much higher in subjects with obstruction of the sinus ostium than in those without (odds ratio = 23.209) in our study. Previous studies have failed to demonstrate a significant association between PSMCs and sinus outflow tract obstruction^(3,4). However, obstruction of the sinus ostium is believed to be the most critical step in developing chronic sinusitis⁽¹²⁾. If PSMCs become large enough to obstruct the sinus ostium, then ventilation and drainage of the involved sinus are blocked, which may result in mucosal thickening, air-fluid levels and finally chronic sinusitis. That is, large PSMCs can lead to ostial obstruction and pooling of secretions in the dependent sinuses. Bacteria then can proliferate within the sinuses, and chronic sinusitis may occur over time. Therefore, subjects with large PSMCs should be informed of their high risk for developing sinusitis and should be followed up regularly.

No data are currently available regarding the association between smoking and the development of PSMCs. In our study, it was found that smoking increased the risk of PSMCs.

Table 4. Association between smoking status and PSMCs.

	Absence of PSMCs	Presence of PSMCs	RR*	95% CI†	p
Smoking status					
Never	3878 (94.0%)	248 (6.0%)	1.00‡		
Former	1570 (91.7%)	143 (8.3%)	1.412	1.140-1.750	0.002
Current	882 (88.9%)	110 (11.1%)	1.939	1.531-2.456	0.000
Allergic rhinitis					
Absence	5857 (92.8%)	452 (7.2%)	1.00§		
Presence	473 (90.6%)	49 (9.4%)	1.293	0.948-1.764	0.105

*RR, relative risk, †CI, confidence interval

‡Risk relative to never smokers adjusted for a history of allergic rhinitis.

§Risk relative to subjects without allergic rhinitis adjusted for smoking status.

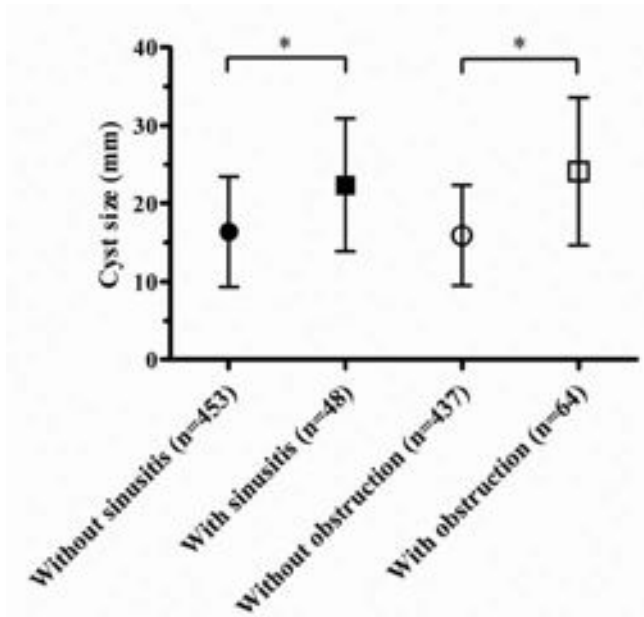


Figure 1. Relationship of cyst size to the presence of sinusitis and the obstruction of the sinus ostium with the cyst. The mean cyst size in subjects with sinusitis was significantly larger than that in those without sinusitis (22.40 ± 8.51 mm vs. 16.41 ± 7.05 mm). In addition, the mean cyst size in subjects with the sinus ostium being obstructed by the cysts was significantly larger than the size in those without (24.14 ± 9.48 mm vs. 15.93 ± 6.43 mm). * $p = 0.000$ by the independent t test.

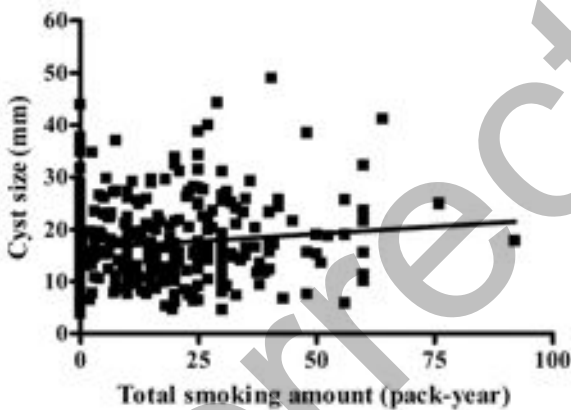


Figure 2. Correlation between total smoking amount and cyst size. Cyst size = $0.056[\text{Total smoking amount}] + 16.356$ ($r^2 = 0.014$, $p = 0.008$).

PSMCs were more commonly found in current and former smokers compared to never smokers. Furthermore, total smoking amount was associated with an increase in cyst size. Cigarette smoke contains many well-known irritants that have been identified as initiators of inflammation. A previous study indicated that cigarette smoking is associated with significant airway inflammation, including vascular hyperplasia, submucosal edema and inflammatory cell infiltrates⁽¹³⁾. Therefore, we believe that PSMCs may arise from inflamed sinus mucosa caused by chronic irritation with smoke. PSMCs rarely cause any symptoms. Similarly, most of the subjects in this study

were asymptomatic. No specific treatment is needed unless patients are symptomatic.

The results of our study are subjected to some limitations. First, there is a possible selection bias because the subjects in this study who underwent MR imaging studies may have a different prevalence of paranasal sinusitis than expected in the general population. Second, subjects included in our study are relatively old.

Our consecutive series of 6,831 brain MR images obtained in subjects who underwent MR imaging for health checkup revealed a prevalence of 7.3% PSMC. Although PSMCs occur across all ages, we found that older age was associated with a decreased prevalence. The results of this study suggest that the size of cysts may be linked with sinus ostium obstruction and subsequent development of sinusitis and that smoking may be an important risk factor for occurrence of PSMCs. Since most subjects with PSMCs were asymptomatic, no specific treatment for PSMCs may be needed.

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The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper.

AUTHORSHIP CONTRIBUTION

Dr Moon and Dr Min had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: IJ Moon and YG Min. Acquisition of data: IJ Moon, JE Lee and ST Kim. Analysis and interpretation of data: IJ Moon, DH Han, CS Rhee and CH Lee. Drafting of the manuscript: IJ Moon and JE Lee. Critical revision of the manuscript for important intellectual content: CS Rhee, CH Lee and YG Min. Statistical analysis: ST Kim and DH Han. Study supervision: YG Min

REFERENCES

1. Kanagalingam J, Bhatia K, Georgalas C, Fokkens W, Mischkiel K, Lund VJ. Maxillary mucosal cyst is not a manifestation of rhinosinusitis: results of a prospective three-dimensional CT study of ophthalmic patients. *Laryngoscope*. 2009; 119: 8-12.
2. Rodrigues CD, Freire GF, Silva LB, Fonseca da Silveira MM, Estrela C. Prevalence and risk factors of mucous retention cysts in a Brazilian population. *Dentomaxillofac Radiol*. 2009; 38: 480-483.
3. Bhattacharyya N. Do maxillary sinus retention cysts reflect obstructive sinus phenomena? *Arch Otolaryngol Head Neck Surg*. 2000; 126: 1369-1371.
4. Harar RP, Chadha NK, Rogers G. Are maxillary mucosal cysts a manifestation of inflammatory sinus disease? *J Laryngol Otol*. 2007; 121: 751-754.
5. Hadar T, Shvero J, Nageris BI, Yaniv E. Mucus retention cyst of the maxillary sinus: the endoscopic approach. *Br J Oral Maxillofac Surg*. 2000; 38: 227-229.
6. Rhodus NL. The prevalence and clinical significance of maxillary sinus mucous retention cysts in a general clinic population. *Ear Nose Throat J*. 1990; 69: 82-87.

7. Berg O, Carenfelt C, Sobin A. On the diagnosis and pathogenesis of intramural maxillary cysts. *Acta Otolaryngol.* 1989; 108: 464-468.
8. Branstetter BFT, Weissman JL. Role of MR and CT in the paranasal sinuses. *Otolaryngol Clin North Am.* 2005; 38: 1279-1299.
9. Carter LC, Calamel A, Haller A, Aguirre A. Seasonal variation in maxillary antral pseudocysts in a general clinic population. *Dentomaxillofac Radiol.* 1998; 27: 22-24.
10. Kaffe I, Littner MM, Moskona D. Mucosal-antral cysts: radiographic appearance and differential diagnosis. *Clin Prev Dent.* 1988; 10: 3-6.
11. Casamassimo PS, Lilly GE. Mucosal cysts of the maxillary sinus: a clinical and radiographic study. *Oral Surg Oral Med Oral Pathol.* 1980; 50: 282-286.
12. Scribano E, Ascenti G, Loria G, Cascio F, Gaeta M. The role of the ostiomeatal unit anatomic variations in inflammatory disease of the maxillary sinuses. *Eur J Radiol.* 1997; 24: 172-174.
13. Roth MD, Arora A, Barsky SH, Kleerup EC, Simmons M,

Tashkin DP. Airway inflammation in young marijuana and tobacco smokers. *Am J Respir Crit Care Med.* 1998; 157: 928-937.

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