

RESEARCH ARTICLE

Chronic rhinosinusitis increases the risk of hemorrhagic and ischemic stroke: A longitudinal follow-up study using a national sample cohort

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Abstract

Background

Several studies have reported that chronic rhinosinusitis (CRS) increases the risk of stroke. The aim of this study is to elucidate the putative association between CRS and stroke (ischemic or hemorrhagic) using large population-based national health insurance data.

Methods

Using the national cohort study from the Korean Health Insurance Review and Assessment Service, CRS patients (n = 22,959) and control participants (n = 91,836) were selected and matched at a rate of 1:4 (age, sex, income, region, hypertension, diabetes, and dyslipidemia). A Cox-proportional hazard model was used to analyze the hazard ratio (HR) of CRS for hemorrhagic stroke and ischemic stroke. We divided the participants according to age and gender for the subgroup analysis.

Results

The HR for hemorrhagic and ischemic stroke was significantly increased in the CRS patients compared to that in the controls (adjusted HR = 2.43, 95% confidence interval [CI] = 2.10–2.80 for hemorrhagic stroke; adjusted HR = 1.76, 95% CI = 1.61–1.92 for ischemic stroke) after adjusting for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder. In the subgroup analysis, the HR of hemorrhagic stroke was significantly increased in the CRS group regardless of age and gender. The HR of ischemic stroke was also significantly increased in all subgroups of the CRS group.

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Conclusion

CRS consistently increased the risk of ischemic and hemorrhagic stroke regardless of age and gender.

Introduction

Chronic rhinosinusitis (CRS) is a prevalent disease defined as inflammation of the nose and the paranasal sinuses lasting more than 12 weeks [1]. Patients with CRS present with symptoms of nasal blockage, rhinorrhea, post-nasal drip, facial pain, or smell disorders. The GA²LEN study reported an overall prevalence of CRS of 10.9% in the European population, [2], while the investigated prevalence of CRS was 14% in the U.S.A [3]. In Korea, 6.2% of the general population was diagnosed with CRS according to a questionnaire and physical examination [4]. CRS is a common chronic disease and is associated with a socioeconomic burden. Rhinosinusitis may lead to life-threatening intracranial complications, such as subdural empyema, cavernous sinus thrombophlebitis, meningitis, and brain abscess [5].

Stroke is an abrupt interruption in cerebral blood flow causing brain cell death followed by neurological deficits. Ischemic and hemorrhagic stroke are the two major stroke types. The modifiable risk factors of stroke include hypertension, smoking, high waist-to-hip ratio, physical inactivity, hyperlipidemia, diabetes mellitus, and alcohol consumption [6].

Recently, several studies based on large population insurance data indicated a close relationship between CRS and stroke [7,8]. The suggested hypotheses for this association were anatomical proximity of the sinus and brain, inflammation-mediated emboli or spasm of cerebral arteries, adverse reactions to an associated allergy medicine, or complications following sinus surgery [7–10].

The aim of this study is to elucidate the putative association between CRS and stroke using large population-based national health insurance data. We identified this association for both hemorrhagic and ischemic stroke.

Methods

Study population and data collection

The ethics committee of Hallym University (2014-I148) approved the use of these data. Written informed consent was exempted by the Institutional Review Board.

This national cohort study relies on data from the Korean Health Insurance Review and Assessment Service-National Sample Cohort (HIRA-NSC). The Korean National Health Insurance Service (NHIS) selects samples directly from the entire population database to prevent non-sampling errors. Approximately 2% of the samples (one million) were selected from the entire Korean population (50 million). These selected data were classified at 1,476 levels (age [18 categories], sex [2 categories], and income level [41 categories]) using randomized stratified systematic sampling methods via proportional allocation to represent the entire population. After data selection, the appropriateness of the sample was verified by a statistician who compared the data from the entire Korean population to the sample data. The details of the methods used to perform these procedures are provided by the National Health Insurance Sharing Service [11]. This cohort database includes (i) personal information, (ii) health insurance claim codes (procedures and prescriptions), (iii) diagnostic codes using the International Classification of Disease-10 (ICD-10), (iv) death records from the Korean National Statistical Office (using the Korean Standard Classification of disease), (v) socioeconomic data (residence

and income), and (vi) medical examination data for each participant over the period ranging from 2002 to 2013.

Because all Korean citizens are recognized by a 13-digit resident registration number from birth to death, exact population statistics can be determined using this database. It is mandatory for all Koreans to enroll in the NHIS. All Korean hospitals and clinics use the 13-digit resident registration number to register individual patients in the medical insurance system. Therefore, the risk of overlapping medical records is minimal, even if a patient moves from one place to another. Moreover, all medical treatments in Korea can be tracked without exception using the HIRA system. In Korea, notice of death to an administrative entity is legally required before a funeral can be held. The causes and date of death are recorded by medical doctors on a death certificate.

Participant selection

Of 1,125,691 cases with 114,369,638 medical claim codes, we included only participants who were diagnosed with chronic sinusitis (ICD-10: J32). Among them, we selected the participants who were treated ≥ 2 times, those who underwent head and neck CT evaluations (Claim codes: HA401-HA416, HA441-HA443, HA451-HA453, HA461-HA463, or HA471-HA473), and those not diagnosed with nasal polyps (J33) ($n = 34,572$). The participants were followed up to 12 years.

The history of admission for hemorrhagic stroke (I60: Subarachnoid hemorrhage, I61: Intracerebral hemorrhage, and I62: Other nontraumatic intracranial hemorrhage) and ischemic stroke (I63: Cerebral infarction) were identified using ICD-10 codes. We selected participants who were treated ≥ 1 time. These methods were used in other studies to evaluate the incidence of stroke in Korea [12,13].

CRS patients were matched at a ratio of 1:4 with participants (control group) who had not been diagnosed with CRS from 2002 through 2013. The participants were matched for age group, sex, income group, region of residence, and past medical history (hypertension, diabetes, and dyslipidemia). To prevent selection bias when selecting the matched participants, the control group participants were sorted by a random order. It was assumed that the matched control participants were involved at the same time as each matched CRS participant (index date). Therefore, participants in the control group who died before the index date were excluded. In both the CRS and control groups, participants who had histories of hemorrhagic or ischemic stroke before the index date were excluded. In the chronic sinusitis group, 540 participants were excluded. CRS patients for whom we could not identify sufficient matching participants were excluded ($n = 119$). We excluded participants under 20 years old ($n = 10,954$). Finally, 1:4 matching resulted in the inclusion of 22,959 CRS patients and 91,836 control participants (Fig 1). However, they were not matched for ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder histories in that strict matching increases the drop out the participant due to lack of control participants.

Variables

Age groups were classified using 5-year intervals: 20–24, 25–29, 30–34. . . , and 85+ years. A total of 14 age groups were designated. The income groups were initially divided into 41 classes (one health aid class, 20 self-employment health insurance classes, and 20 employment health insurance classes). These groups were re-categorized into 11 classes (class 1 [lowest income]-11 [highest income]). Region of residence was divided into 16 areas according to administrative district. These regions were regrouped into urban (Seoul, Busan, Daegu, Incheon,

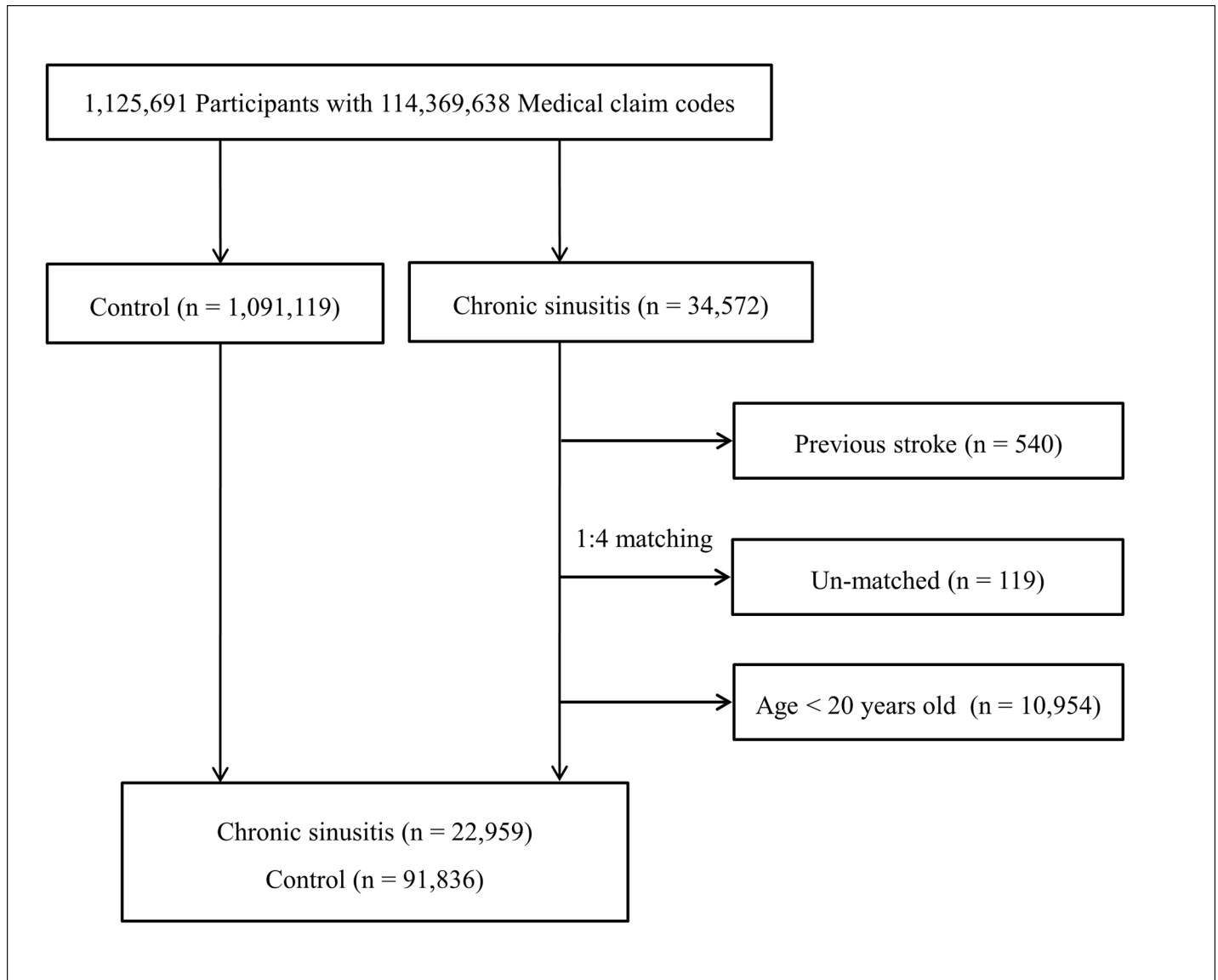


Fig 1. A schematic illustration of the participant selection process that was used in the present study. Of 1,125,691 cases with 114,369,638 medical claim codes, 34,572 CRS participants were selected. The participants of previous stroke history were excluded (n = 540). The CRS participants were matched 1:4 with a control group who had not been diagnosed with CRS. Un-matched CRS participants (n = 119) and less than 20 years old participants (n = 10,954) were excluded. Finally, 22,959 CRS participants and 91,836 control participants were included.

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Gwangju, Daejeon, and Ulsan) and rural areas (Gyeonggi, Gangwon, Chungcheongbuk, Chungcheongnam, Jeollabuk, Jeollanam, Gyeongsangbuk, Gyeongsangnam, and Jeju).

The past medical histories of participants were evaluated using ICD-10 codes. For the accuracy of diagnosis, hypertension (I10 and I15), diabetes (E10-E14), dyslipidemia (E78), migraine (G43), and chronic kidney disease (N18) were evaluated for participants who were treated ≥ 2 times. Ischemic heart disease (I20 and I25) were check if the participants were treated ≥ 1 time. Depression was defined F31 (bipolar affective disorder) through F39 (unspecified mood disorder) who treated ≥ 2 times by a psychiatrist. Sleep disorder was defined G47 who treated ≥ 2 times. Chronic obstructive pulmonary disease (COPD) was defined following the previous study [14].

Statistical analysis

A chi-square test was used to compare the general characteristics between the CRS and control groups.

A Cox-proportional hazard model was used to calculate the hazard ratio (HR) of CRS for stroke (hemorrhagic or ischemic). In these analyses, crude (simple) and adjusted (age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder) models were used. We calculated the HR and 95% confidence interval (CI). For the subgroup analysis, we divided the participants by age and sex (20–39 years old, 40–59 years old, 60+ years old; men and women). We performed other subgroup analyses according to follow up periods (≤ 1 year, ≤ 3 years, and ≤ 5 years).

Two-tailed analyses were conducted, and *P* values less than 0.05 were considered to indicate statistical significance. The results were statistically analyzed using SPSS v. 21.0 (IBM, Armonk, NY, USA).

Results

Mean interval from index date through outcome (hemorrhagic stroke) was 50.7 months \pm 35.1 in CRS group and 51.4 \pm 35.4 months in control. In ischemic stroke, it was 48.8 \pm 35.1 months in CRS group and 49.9 \pm 34.8 months in control. The general characteristics of the control group were exactly matched with those of the CRS group. However, the prevalence of stroke (hemorrhagic or ischemic), ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder were significantly increased in the CRS group ($P < 0.001$) (Table 1).

In the Cox-proportional hazard regression model, the crude HRs of hemorrhagic stroke and ischemic stroke were 2.43 (95% CI = 2.11–2.79) and 1.78 (95% CI = 1.64–1.94), respectively, in the CRS group, which were statistically significant. After adjusting for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder, the HRs for both subtypes of stroke were still significantly increased in the CRS group (adjusted HR = 2.43, 95% CI = 2.10–2.80 for hemorrhagic stroke; adjusted HR = 1.76, 95% CI = 1.61–1.92 for ischemic stroke) (Table 2).

In the subgroup analysis, the HR of hemorrhagic stroke was significantly increased in the CRS group regardless of age and sex. For example, middle-aged (40–59 years) men with CRS had a 3.23-fold (crude HR = 3.20) increased risk of hemorrhagic stroke compared to the control group (95% CI = 2.32–4.49, $P < 0.001$). The HR of ischemic stroke was also significantly increased in all subgroups of the CRS group (Table 3).

The adjusted HR of hemorrhagic stroke was 2.00 (95% CI = 1.36–2.95) within 1 year and 2.24 (95% CI = 1.87–2.69) within 5 years. For ischemic stroke, the adjusted HR was 1.50 (95% CI = 1.20–1.88) within 1 year and 1.75 (95% CI = 1.57–1.95) within 5 years of follow-up (each of $P < 0.001$, Table 4).

Discussion

CRS increased the risk of hemorrhagic and ischemic stroke in the present study. In the subgroup analyses according to age and sex, the risk of stroke was consistently increased in CRS participants.

Most CRS cases and complications are usually mild and self-limiting. However, cerebral complications (subdural empyema, meningitis, cavernous sinus thrombophlebitis, and brain abscess) caused by CRS can be associated with severe sequelae, as they can be disabling in 25%

Table 1. General characteristics of participants.

Characteristics	Total participants		
	CRS (n, %)	Control (n, %)	P-value
Age (years old)			1.000
20–24	1,329 (5.8)	5,316 (5.8)	
25–29	1,770 (7.7)	7,080 (7.7)	
30–34	2,200 (9.6)	8,800 (9.6)	
35–39	2,332 (10.2)	9,328 (10.2)	
40–44	2,318 (10.1)	9,272 (10.1)	
45–49	2,474 (10.8)	9,896 (10.8)	
50–54	2,526 (11.0)	10,104 (11.0)	
55–59	2,257 (9.8)	9,028 (9.8)	
60–64	1,894 (8.2)	7,576 (8.2)	
65–69	1,705 (7.4)	6,820 (7.4)	
70–74	1,165 (5.1)	4,660 (5.1)	
75–79	654 (2.8)	2,616 (2.8)	
80–84	248 (1.1)	992 (1.1)	
85+	87 (0.4)	348 (0.4)	
Sex			1.000
Male	9,589 (41.8)	38,356 (41.8)	
Female	13,370 (58.2)	53,480 (58.2)	
Income			1.000
1 (lowest)	383 (1.7)	1,532 (1.7)	
2	1,383 (6.0)	5,532 (6.0)	
3	1,465 (6.4)	5,860 (6.4)	
4	1,508 (6.6)	6,032 (6.6)	
5	1,669 (7.3)	6,676 (7.3)	
6	1,868 (8.1)	7,472 (8.1)	
7	2,067 (9.0)	8,268 (9.0)	
8	2,443 (10.6)	9,772 (10.6)	
9	2,825 (12.3)	11,300 (12.3)	
10	3,228 (14.1)	12,912 (14.1)	
11 (highest)	4,120 (17.9)	16,480 (17.9)	
Region of residence			1.000
Urban	11,300 (49.2)	45,200 (49.2)	
Rural	11,659 (50.8)	46,636 (50.8)	
Hypertension			1.000
Yes	8,648 (37.7)	34,592 (37.7)	
No	14,311 (62.3)	57,244 (62.3)	
Diabetes			1.000
Yes	4,796 (20.9)	19,184 (20.9)	
No	18,163 (79.1)	72,652 (79.1)	
Dyslipidemia			1.000
Yes	7,465 (32.5)	29,860 (32.5)	
No	15,494 (67.5)	61,976 (67.5)	
Ischemic heart disease			<0.001*
Yes	1,855 (8.1)	5,458 (5.9)	
No	21,104 (91.9)	86,378 (94.1)	
Migraine			<0.001*
Yes	3,271 (14.2)	5,835 (6.4)	

(Continued)

Table 1. (Continued)

Characteristics		Total participants		
		CRS (n, %)	Control (n, %)	P-value
	No	19,688 (85.8)	86,001 (93.6)	
Chronic kidney disease				<0.001*
	Yes	320 (1.4)	1,024 (1.1)	
	No	22,639 (98.6)	90,812 (98.9)	
Depression				<0.001*
	Yes	3,790 (16.5)	8,304 (9.0)	
	No	19,169 (83.5)	83,532 (91.)	
COPD				<0.001*
	Yes	2,673 (11.6)	5,867 (6.4)	
	No	20,286 (88.4)	85,969 (93.6)	
Sleep disorder				<0.001*
	Yes	2,418 (10.5)	5,215 (5.7)	
	No	20,541 (89.5)	86,621 (94.3)	
Hemorrhagic stroke				<0.001*
	Yes	312 (1.4)	517 (0.6)	
	No	22,647 (98.6)	91,319 (99.4)	
Ischemic stroke				<0.001*
	Yes	756 (3.3)	1,712 (1.9)	
	No	22,203 (96.7)	90,124 (98.1)	

COPD: chronic obstructive pulmonary disorder

*Chi-square test or Fisher’s exact test. Significance at P < 0.05

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of cases and even lead to death in 10% of cases [15,16]. Mechanisms of cerebral complications following CRS have been suggested. The direct invasion of the CRS pathogen through congenital or acquired bony destruction could be one possible pathway. Hematogenous spread (valveless veins or arterial emboli) might be another possible pathway for cerebral complications of CRS [17]. However, sufficient evidence to support the association between CRS and stroke is lacking.

Several case reports have suggested that stroke is related to sinusitis [10,18,19]. Based on this putative association, two nationwide population-based studies recently reported the association between sinusitis and stroke. Wu et al. found that patients with CRS have a 1.39-fold increased risk of stroke compared to controls during a 3-year follow-up period [7]. In our

Table 2. Crude and adjusted hazard ratios (95% confidence interval) of chronic sinusitis for hemorrhagic stroke and ischemic stroke.

Characteristics	Hemorrhagic stroke				Ischemic stroke			
	Crude	P-value	Adjusted†	P-value	Crude	P-value	Adjusted†	P-value
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
	Yes	2.43 (2.11–2.79)	2.43 (2.10–2.80)		1.78 (1.64–1.94)		1.76 (1.61–1.92)	
	No	1.00	1.00		1.00		1.00	

* Cox-proportional hazard regression model, Significance at P < 0.05

† Adjusted model for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder histories

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Table 3. Subgroup analysis of crude and adjusted hazard ratios (95% confidence interval) of chronic sinusitis for hemorrhagic stroke and ischemic stroke according to age and sex.

Characteristics	Hemorrhagic stroke				Ischemic stroke			
	Crude	P-value	Adjusted†	P-value	Crude	P-value	Adjusted†	P-value
Young men (20–39 years old, n = 16,560)								
Chronic sinusitis		0.013*		0.077		<0.001*		<0.001*
Yes	2.23 (1.18–4.19)		1.81 (0.94–3.51)		2.97 (1.66–5.29)		2.89 (1.60–5.22)	
No	1.00		1.00		1.00		1.00	
Young women (20–39 years old, n = 21,595)								
Chronic sinusitis		0.005*		0.005*		<0.001*		0.003*
Yes	2.47 (1.32–4.60)		2.49 (1.32–4.71)		3.59 (1.87–6.90)		2.83 (1.43–5.60)	
No	1.00		1.00		1.00		1.00	
Middle aged men (40–59 years old, n = 19,715)								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	3.20 (2.32–4.42)		3.23 (2.32–4.49)		2.25 (1.81–2.80)		2.19 (1.75–2.73)	
No	1.00		1.00		1.00		1.00	
Middle aged women (40–59 years old, n = 28,160)								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	3.06 (2.24–4.17)		2.96 (2.15–4.07)		1.88 (1.47–2.42)		1.82 (1.41–2.36)	
No	1.00		1.00		1.00		1.00	
Old men (60+ years old, n = 11,670)								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	1.99 (1.48–2.68)		1.98 (1.46–2.68)		1.59 (1.36–1.85)		1.58 (1.35–1.85)	
No	1.00		1.00		1.00		1.00	
Old women (60+ years old, n = 17,095)								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	2.05 (1.56–2.69)		2.13 (1.61–2.81)		1.69 (1.47–1.95)		1.66 (1.43–1.91)	
No	1.00		1.00		1.00		1.00	

* Cox-proportional hazard regression model, Significance at P < 0.05

† Adjusted model for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder histories

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study, the CRS patients had a 2.43-fold increased risk of hemorrhagic stroke and a 1.76-fold increased risk of ischemic stroke compared to the control group. These consistent results support the association between CRS and stroke. Kang et al. reported that during a 5-year follow-up period, ischemic and unspecified stroke were significantly more prevalent in CRS patients. However, no difference was observed in the prevalence of intracerebral hemorrhage in CRS patients [8]. This is different from our results. Our study showed that the risk of hemorrhagic stroke was also significantly increased in CRS patients. This discrepancy may be due to differences in follow-up periods. The progression of CRS is slow and gradual, and a long time is likely necessary to observe intracranial complications such as stroke. Our study had a longer follow-up period than the other study (10 years vs 5 years).

In the subgroup analysis, the risk of stroke showed a definitive relationship with CRS in all groups. The incidence of stroke increases with age and is higher in females after 55 years of age

Table 4. Subgroup analysis of crude and adjusted hazard ratios (95% confidence interval) of chronic sinusitis for hemorrhagic stroke and ischemic stroke according to follow up periods.

Characteristics	Hemorrhagic stroke				Ischemic stroke			
	Crude	P-value	Adjusted†	P-value	Crude	P-value	Adjusted†	P-value
Within 1 year								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	2.08 (1.42–3.03)		2.00 (1.36–2.95)		1.50 (1.20–1.87)		1.50 (1.20–1.88)	
No	1.00		1.00		1.00		1.00	
Within 3 years								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	2.47 (2.00–3.05)		2.45 (1.96–3.04)		1.70 (1.49–1.93)		1.68 (1.47–1.92)	
No	1.00		1.00		1.00		1.00	
Within 5 years								
Chronic sinusitis		<0.001*		<0.001*		<0.001*		<0.001*
Yes	2.29 (1.91–2.73)		2.24 (1.87–2.69)		1.77 (1.59–1.97)		1.75 (1.57–1.95)	
No	1.00		1.00		1.00		1.00	

* Cox-proportional hazard regression model, Significance at P < 0.05

† Adjusted model for age, sex, income, region of residence, hypertension, diabetes, dyslipidemia, ischemic heart disease, migraine, chronic kidney disease, depression, sleep disorder, and chronic obstructive pulmonary disorder histories

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[20]. However, our results showed that CRS patients have a higher likelihood of stroke regardless of age or gender. The HR of stroke was smaller in 60+ year old group compare to that of in <40 and 40–59 years old group (Table 3). Old age may render increased exposure to risk factors of stroke such as cardiovascular problems. At young ages, CRS may be an important risk factor for the development of stroke. Moreover, the HR of stroke was increased over time following CRS and was significantly increased within 1 year (Table 4). This finding supports the causal relationship of the development of stroke following CRS. Considering these findings, early and aggressive CRS treatment may prevent stroke and its accompanying complications.

There are several hypotheses to explain the causal relationship between CRS and stroke. The sphenoid and posterior ethmoid sinus share anatomical proximity with the internal carotid artery. The adjacent sinus and internal carotid artery are separated by an approximately 0.1-mm thin bony wall, and carotid artery bulging into the sinus was found in 8% of patients with CRS [21]. Infectious aneurysms resulting from distal vessel wall involvement of pathogen may cause intracranial hemorrhage or cerebral infarction [22].

The inflammatory cytokines of CRS, such as interleukin-1 and C-reactive protein, are also speculated to play a role in the development of stroke [23,24]. Interleukin-1 may result in perivascular inflammation and progress to thrombosis of the internal carotid artery [18]. Elevated C-reactive protein levels were associated with ischemic stroke in a meta-analysis [25].

In many previous epidemiologic studies, CRS showed a strong association with cigarette smoking [26,27]. The mucociliary clearance of the sinuses is disturbed by tobacco smoke, which subsequently increases inflammation [28]. Cigarette smoking is a major risk factor for stroke that exhibits a dose-response relationship and contributes to a stroke mortality rate of approximately 15% [29,30]. The hazardous effects of cigarette smoking may explain the relationship between CRS and stroke.

Oral decongestant is commonly used to relieve symptoms of nasal obstruction in CRS. It increases the systolic blood pressure and heart rate, which may increase the risk of stroke [31].

As an example, from 2002 to 2004, the exposure rate of phenylpropanolamine which is associated with hemorrhagic stroke was 0.6% to 1.6% among hospital visiting patients in Korea [32]. Intracranial hemorrhage is a rare cerebral complication after functional endoscopic sinus surgery that is performed to treat CRS. The treatment modalities for alleviating the symptoms of CRS could be causes of stroke, though their contributions were not precisely assessed.

Our study has an advantage over previous nation-wide studies. First, the duration of the follow-up period was 3 to 5 years in previous large population-based studies. We followed the study population for 10 years, which would allow sufficient time for the progression of stroke following CRS. In addition, we performed subgroup analysis according to follow-up duration. Second, the control group was matched not only for the basic characteristics of the CRS group but also for risk factors of stroke, such as hypertension, diabetes and dyslipidemia. This detailed matching might provide valid evidence for the effect of CRS on stroke.

This study has several limitations. Although this study used a representative large population and was matched and adjusted for possible confounders, other confounders were still present, such as cardiovascular comorbidities, emotional disorders, smoking, alcohol intake, and drug usage. In addition, the degree of sinusitis was not considered in the present study. Similarly, the durations and severities of sinusitis were not consistent among the study population. In addition, missed diagnoses could not be excluded. Only CRS patients who were diagnosed by clinicians were included in this study. We did not examine the medication histories of participants.

Conclusion

In conclusion, CRS consistently increases the risk of ischemic and hemorrhagic stroke regardless of age and gender.

Author Contributions

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