Association between body composition indices and prevalence of chronic rhinosinusitis in Koreans*

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To the Editor:

The World Health Organization has recently reported that the worldwide prevalence of obesity has tripled since 1975. In 2016 39% of adults were overweight and 13% were obese [(1)]. While there are established associations between obesity and chronic diseases such as cardiovascular disease, type 2 diabetes, and asthma, there has yet to be a consensus on the association of obesity with CRS. Previous studies that have used body mass index (BMI) as a metric for obesity have reported inconsistent results [(2,3)]. BMI measures total body mass, including both fat and lean mass, thus it is considered a poor measure of adiposity. We decided studying body composition and fat distribution separately as they could contribute differently to the immunologic response [(4)]. We studied the association between the distribution of fat mass and lean (fat-free) mass in the body and its effect on the prevalence of CRS.

Using the Korea National Health and Nutrition Examination Survey (KNHANES), we investigated the relative contribution of various body composition parameters to the prevalence of CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSsNP) in men and women. In addition, we investigated the role of fat or lean mass contributing to atopy via serum Immunoglobulin E levels.

KNHANES is a nationwide survey designed to represent the non-industrialized South Korean population, using a stratified, multistage clustered sampling method. Out of 19,491 participants who participated in the fifth KNHANES in 2009-2010, 6,770 participants were excluded with the following criteria; <18 years of age, those who did not undergo nasal endoscopic examination, those whose body composition data was not available, and those in whom conditions other than nasal polyps were suspected on endoscopy. This study was approved by the Institutional Review Board of the Korean Center for Disease Control and Prevention, (2009-02CON-03-2C, 2010-02CON-21-C).

We defined CRS using the definition from the epidemiological section of the European position paper on rhinosinusitis and nasal polyps, as well as endoscopic findings of nasal polyps or pus within the middle meatus. Participants were classified into the CRSwNP and CRSsNP groups Consequently, 12,721 participants were enrolled in this study, of whom 322 and 368 participants were assigned to the CRSwNP and CRSsNP groups, respectively.

In KNHANES 2009-2010, whole-body dual-energy X-ray absorptiometry (DXA) was performed in all participants to determine the total and regional body fat mass and lean mass. In this study, the following body composition indices were calculated: total weight for BMI, total fat mass weight for fat mass index (FMI), total lean mass weight for lean mass index (LMI), and appendicular lean mass weight for appendicular LMI (ALMI). Additionally, the ratio of trunk fat percentage (fat mass/total mass × 100) to total fat percentage (trunk-to-total fat ratio) was determined. The Supplementary note 1 provides a detailed explanation of the methods.

The prevalence of CRS phenotypes and the tertile classification of each body composition parameter is shown in Figure 1. The prevalence of CRSwNP tended to increase with trunk-to-total ratio in men (Figure 1A) while CRSwNP prevalence increased with all the parameters measured in women (Figure 1C). As for CRSsNP, the prevalence showed no significant association with any parameter in men (Figure 1B) whereas the prevalence tended to decrease with BMI and trunk-total fat ratio in women (Figure 1D). The comparison of body composition parameters between the control and CRS phenotypes according to sex is described in Supplementary Table 1.

Under univariable logistic regression analysis (Supplementary Table 2), a lower prevalence of CRSwNP was associated with a low trunk-to-total fat ratio in men (odds ratio [OR]=0.63, p-value=0.021), while all the body composition indices, except ALMI, were positively associated with CRSwNP in women. The lower prevalence of CRSsNP was associated with lower trunk-total fat ratio in men (OR=0.69, p-value=0.045) while none of the

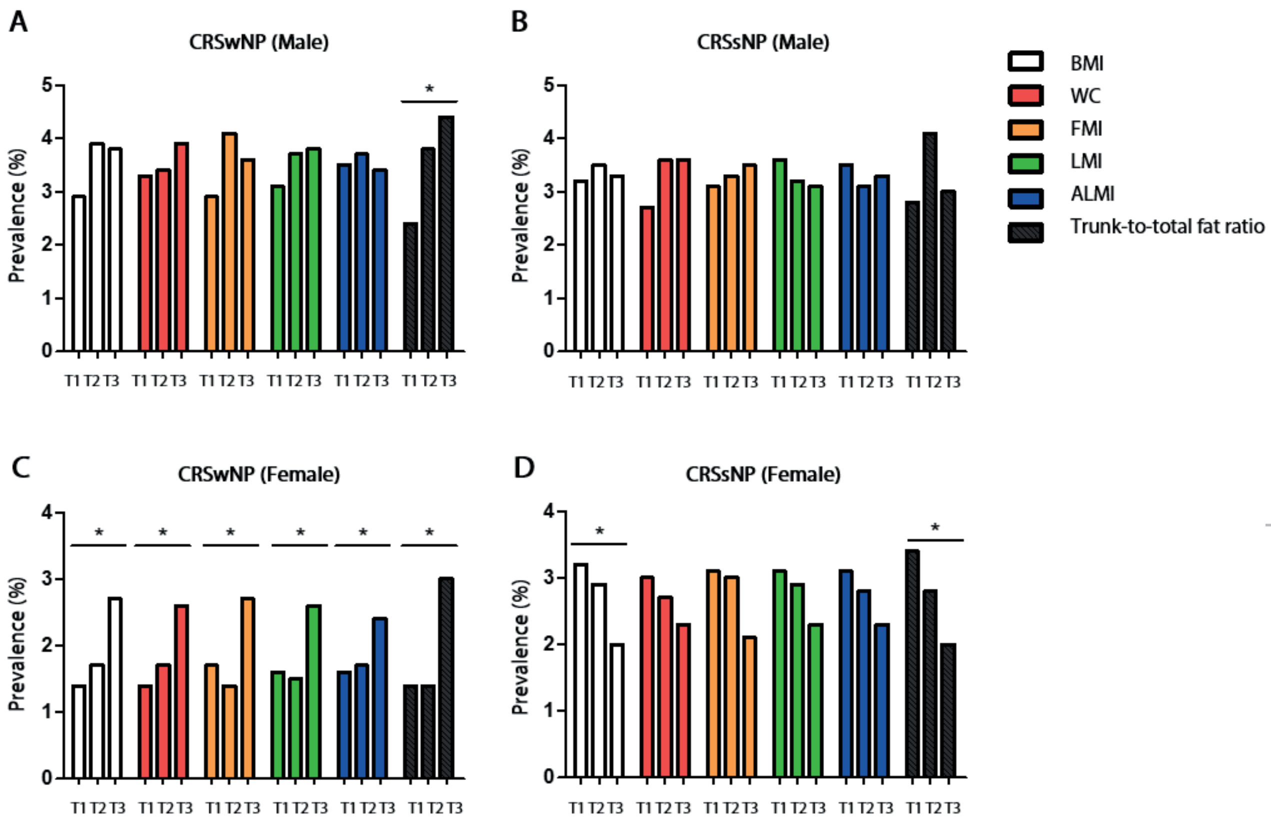

Figure 1. Prevalence of chronic rhinosinusitis with nasal polyps (A, C) and without nasal polyps (B, D) in males (A, B) and females (C, D), respectively, according to each body composition index by tertile (A) (*p for trend<0.05)
Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; CRSsNP, chronic rhinosinusitis without nasal polyps; BMI, body mass index; WC, waist circumference; FMI, fat mass index; LMI, lean mass index; ALMI, appendicular lean mass index.

measured parameters had a statistically significant association with CRSsNP prevalence in women.
The multivariate logistic regression analysis for the association between body composition parameters and each CRS phenotype according to sex is shown in Table 1. The lower prevalence of CRSwNP was associated with low trunk-to-total fat ratio (OR=0.60, p-value=0.012) in men , and higher prevalence of CRSwNP showed a significant assocation with a high trunk-to-total fat ratio in women (OR=1.81, p-value=0.007). In addition, a high FMI (OR=1.70, p-value=0.018) and LMI (OR=1.58, p-value=0.035) were also associated with a higher prevalence of CRSwNP in women. As for CRSsNP, the lower prevalence was associated with low trunk-to-total fat ratio in men (OR=0.62, p=0.012). In women, none of the parameters showed a statistically significant association with CRSsNP prevalence.

Our study revealed that a high percentage of truncal fat was associated with sinonasal inflammation in both sexes, although visceral and subcutaneous abdominal fat could not be clearly distinguished due to the nature of DXA. These results show consistency with previous studies on asthma, reporting that greater abdominal obesity, either visceral or subcutaneous adiposity, correlates with disease severity [5,6]. The impact of the LMI on CRSwNP in women might be due to the contribution of excess ectopic fat rather than greater muscular mass on lean mass assessment by DXA [7]. Leptin, a classic proinflammatory adipokine, has been reported to be present in normal nasal mucosa as well as in nasal polyps and to promote interleukin (IL)-13 induced mucin hypersecretion, suggesting the possible role of adipose tissue in CRS pathogenesis [8].
CRSwNP, which is often associated with Th2 inflammation, was more clearly associated with the trunk-to-total fat mass ratio than CRSsNP. This suggests that the truncal fat proportion contributes to Th2 inflammation in the pathogenesis of CRSwNP, supporting previous reports of higher Th2 cytokine level in the central obesity population compared to population with general obesity [9]. However, owing to the nature of the nationwide survey, it was not possible to confirm the endotype of CRS.

In conclusion, the study results support the association between central obesity and CRSwNP in South Korean adults. Additionally, women with higher FMI and LMI had a higher prevalence of CRSwNP than men, suggesting that there are differences in the effects of body composition on this disease according to sex.

Table 1. Multivariable logistic regression analysis for the association between body composition parameters and chronic rhinosinusitis with or without nasal polyps according to sex.

		Adjusted odds ratio (95% CI)[a]			
		CRSwNP		CRSsNP	
Variables	Tertile	Male	Female	Male	Female
BMI (kg/m²)	1	0.66* (0.45–0.96)	0.97 (0.60–1.57)	0.84 (0.57–1.22)	1.00 (0.71–1.42)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.05 (0.74–1.49)	1.43 (0.95–2.15)	0.96 (0.66–1.38)	0.77 (0.53–1.13)
WC (cm)	1	1.02 (0.70–1.49)	1.04 (0.65–1.67)	0.71 (0.48–1.05)	0.90 (0.63–1.29)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.20 (0.83–1.72)	1.23 (0.81–1.87)	1.08 (0.76–1.55)	0.95 (0.65–1.38)
FMI (kg/m²)	1	0.70 (0.48–1.13)	1.46 (0.91–2.35)	0.85 (0.58–1.25)	0.97 (0.69–1.37)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	0.89 (0.63–1.27)	1.70* (1.10–2.63)	1.07 (0.74–1.54)	0.79 (0.54–1.15)
LMI (kg/m²)	1	0.74 (0.50–1.07)	1.29 (0.81–2.06)	1.12 (0.78–1.63)	0.93 (0.66–1.32)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.13 (0.79–1.61)	1.58* (1.03–2.42)	1.01 (0.69–1.48)	0.82 (0.57–1.19)
ALMI (kg/m²)	1	0.81 (0.56–1.17)	1.00 (0.64–1.58)	1.11 (0.76–1.62)	1.02 (0.72–1.44)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.03 (0.71–1.48)	1.35 (0.90–2.04)	1.08 (0.74–1.58)	0.89 (0.61–1.29)
Trunk-to-total fat ratio	1	0.60* (0.40–0.89)	1.30 (0.78–2.18)	0.62* (0.42–0.90)	1.06 (0.72–1.50)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.16 (0.83–1.63)	1.81* (1.18–2.80)	0.78 (0.54–1.12)	0.78 (0.52–1.17)

[a] Adjusted for age, residency, income, smoking habit, alcohol habit, exercise, hypertension, and diabetes. Abbreviations: CI, confidential intervals; CRSwNP, chronic rhinosinusitis with nasal polyp; CRSsNP, chronic rhinosinusitis without nasal polyp; BMI, body mass index; WC, waist circumference; FMI, fat mass index; LMI, lean mass index; ALMI, appendicular lean mass index. *p-value < 0.05.

Conflict of interest

There are no competing interests.

Authorship contribution

THK and KL had full access to all of the data in the study and takes responsibility or the integrity of the data and the accuracy of the data analysis. Concept and design: THK, KJL; Acquisition, analysis, or interpretation of data: All authors; Drafting of the manuscript: KL, KK; Critical revision of the manuscript for important intellectual content: SHL, THK; Statistical analysis: KK; Obtained funding: THK; Administrative, technical, or material support: KL; Study supervision: THK.

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This manuscript contains online supplementary material

SUPPLEMENTARY MATERIAL

Materials and methods

Data used for the study and study population

This cross-sectional study used the data from the fifth edition of Korea National Health and Nutrition Examination Survey (2009–2010), a nationwide, population-based survey organized by the Korean Center for Disease Control and Prevention. This survey was designed to represent the non-industrialized South Korean population using a complex, stratified, multistage clustered sampling method, including a health interview, physical examination, and nutritional reports. The Korean Society of Otorhinolaryngology-Head and Neck Surgery participated in this survey from 2008–2012, and 150 residents trained in the otorhinolaryngology departments of 47 institutes conducted medical interviews and physical examinations in a standardized manner. Written informed consent was provided by all the participants. The Institutional Review Board of the Korean Center for Disease Control and Prevention approved this study (2009-02CON-03-2C, 2010-02CON-21-C) in accordance with the ethical principles for medical research involving human subjects defined by the Declaration of Helsinki.

Out of a total of 19,491 participants, 6,770 participants, i.e., those aged <18 years, those who did not undergo nasal endoscopic examination, those whose body composition data was not available, and those in whom tumorous conditions other than nasal polyps were suspected on endoscopy, were excluded. The mean participant age in the CRSwNP, CRSsNP, and control groups was 55.41±14.85, 46.33±16.40, and 49.30±16.27, respectively.

Definition of sinonasal inflammatory diseases

We defined CRS using the definition from the epidemiological section of the European study on rhinosinusitis and nasal polyps. CRS was diagnosed when the participants experienced more than two of the four symptoms indicating sinusitis (nasal obstruction, anterior/posterior nasal drip, facial pain/pressure, and olfactory dysfunction) and experienced at least one nasal obstruction or anterior/posterior nasal drip for a minimum of 12 weeks, or were diagnosed with nasal polyps on endoscopy. Participants were further classified into the CRSwNP and CRSsNP groups according to the presence of nasal polyps.

In 2010, the ImmunoCAP 100 (Thermo Fisher Scientific, Uppsala, Sweden) was conducted in 10% of the total participants to measure the serum total IgE levels and specific IgE levels for three common indoor allergens (Dermatophagoides farinae, cockroaches, and dogs). The cutoff values for the serum total and specific IgE levels were defined as 100 kU/L and 0.35 kU/L.

Measurement of body composition

BMI was calculated from the body weight and height (kg/m2), and waist circumference (WC) was measured at the midpoint between the lower border of the rib cage and the iliac crest in the standing position. Whole-body DXA (QDR 4500A fan beam densitometer, Hologic Inc., Bedford, MA, USA) was performed by well-trained technicians to determine the total and regional body fat mass and lean mass.

The following body composition indices were calculated using the height and weight: total weight for BMI, total fat mass weight for fat mass index (FMI), total lean mass weight for lean mass index (LMI), and appendicular lean mass weight for appendicular LMI (ALMI). Additionally, the ratio of trunk fat percentage (fat mass/total mass × 100) to total fat percentage (trunk-to-total fat ratio) was determined. Using these parameters, participants were classified into 3 groups based on the tertiles for each variable.

Assessment of variables

Data regarding age, residency, household income, smoking, alcohol consumption, exercise, and presence of hypertension and diabetes were collected. Participants were classified into two groups (urban and rural) based on residency. Household income was categorized into groups by quartile. Participants were also classified into groups according to their current active smoking status, whether they drank >4 times a week, and whether they performed moderate exercise for a least 30 minutes on >5 days a week. The presence of hypertension and diabetes were defined according to the history of a diagnosis as reported by the participants in the questionnaire.

Statistical analyses

Statistical Analysis System (SAS) version 9.4 (SAS Institute, Inc., Cary, NC, USA) was used to perform the statistical analysis. The baseline characteristics of the participants were described using means and standard errors or as proportions. The baseline characteristics of the participants with CRS and controls were compared using the Student t-test and chi-square test. Univariate and multivariate logistic regression analyses were performed to evaluate the association between each body composition index and CRS. The confounding factors included age, residency, household income, smoking habit, alcohol habit, exercise, and the presence of hypertension and diabetes.

Supplementary Table 1. Comparison of body composition parameters between the control and chronic rhinosinusitis phenotypes according to sex.

	Male (n=5,505)			Female (n=7,216)		
	Control (n=5,142)	CRSwNP (n=188)	CRSsNP (n=175)	Control (n=6,889)	CRSwNP (n=134)	CRSsNP (n=193)
BMI (kg/m^2)	23.95±3.15	24.18±3.20	23.96±3.04	23.37±3.46	24.24±3.70	23.05±3.60
WC (cm)	84.24±8.96	85.11±8.76	85.17±8.53	78.48±9.88	81.17±11.01	77.48±9.58
FMI (kg/m^2)	5.41±1.82	5.49±1.75	5.51±1.74	7.84±2.24	8.27±2.45	7.64±2.18
LMI (kg/m^2)	18.31±1.88	18.46±1.93	18.21±1.80	15.34±1.65	15.74±1.83	15.17±1.72
ALMI (kg/m^2)	7.64±0.91	7.64±0.96	7.60±0.91	5.87±0.74	6.01±0.83	5.79±0.77
Trunk-to-total fat ratio	1.09±0.08	1.11±0.07	1.10±0.08	1.00±0.09	1.02±0.09	0.98±0.09

Abbreviations: CRSwNP, chronic rhinosinusitis with nasal polyps; CRSsNP, chronic rhinosinusitis without nasal polyps; BMI, body mass index; WC, waist circumference; FMI, fat mass index; LMI, lean mass index; ALMI, appendicular lean mass index.

Supplementary Table 2. Univariable logistic regression analysis for the association between body composition parameters and chronic rhinosinusitis with or without nasal polyps according to sex.

		Crude odds ratio (95% CI)			
		CRSwNP		CRSsNP	
Variables	Tertile	Male	Female	Male	Female
BMI (kg/m^2)	1	0.73 (0.51–1.06)	0.82 (0.51–1.31)	0.91 (0.63–1.32)	1.11 (0.79–1.54)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	0.98 (0.70–1.39)	1.63* (1.09–2.44)	0.95 (0.66–1.37)	0.69 (0.48–1.00)
WC (cm)	1	0.95 (0.66–1.36)	0.83 (0.52–1.31)	0.73 (0.50–1.07)	1.03 (0.738–1.45)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.15 (0.81–1.64)	1.53* (1.02–2.29)	1.02 (0.71–1.45)	0.80 (0.56–1.15)
FMI (kg/m^2)	1	0.70 (0.49–1.01)	1.25 (0.78–2.00)	0.94 (0.65–1.37)	1.04 (0.75–1.46)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	0.86 (0.61–1.21)	1.96* (1.28–3.02)	1.07 (0.74–1.54)	0.71 (0.49–1.02)
LMI (kg/m^2)	1	0.84 (0.58–1.21)	1.09 (0.68–1.73)	1.15 (0.79–1.65)	1.06 (0.76–1.48)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.05 (0.74–1.48)	1.76* (1.16–2.68)	0.98 (0.67–1.43)	0.77 (0.54–1.11)
ALMI (kg/m^2)	1	0.97 (0.68–1.38)	0.92 (0.59–1.45)	1.15 (0.79–1.67)	1.13 (0.80–1.58)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	0.92 (0.64–1.31)	1.44 (0.95–2.16)	1.09 (0.75–1.59)	0.84 (0.59–1.21)
Trunk-to-total fat ratio	1	0.63* (0.43–0.93)	1.00 (0.61–1.64)	0.69* (0.47–1.00)	1.24 (0.89–1.72)
	2	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	3	1.17 (0.84–1.63)	2.22* (1.46–3.39)	0.73 (0.51–1.05)	0.69 (0.47–1.01)

Abbreviations: CI, confidential intervals; CRSwNP, chronic rhinosinusitis with nasal polyp; CRSsNP, chronic rhinosinusitis without nasal polyp; BMI, body mass index; WC, waist circumference; FMI, fat mass index; LMI, lean mass index; ALMI, appendicular lean mass index. *p-value<0.05.