

Osteoarthritis and Cartilage



Association between serum immunoglobulin E levels and knee osteoarthritis in Korean adults



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SUMMARY

Objective: The objective of this study was to examine whether osteoarthritis (OA) in the knees was associated with total immunoglobulin E (IgE), allergen-specific IgE, or allergic sensitizations in a nationally representative population.

Methods: The study population comprised of 785 adults aged 50 years or more in the Korea National Health and Nutrition Examination Survey 2010. OA was diagnosed as radiographic (rOA) and symptomatic osteoarthritis (sxOA). We performed multivariable logistic regression analyses to investigate relationships of OA in a knee with serum total IgE, allergen (*Dermatophagoides farinae*, cockroach, and dog allergens)-specific IgE, and allergic sensitizations.

Results: Participants with the highest tertile of the total IgE had 92% and 242% increased risk of knee rOA and sxOA, respectively. Those with *D. farinae*-specific IgE had 2.2 times increased risk of knee sxOA compared to the lowest tertile. Participants with high total IgE (>150kU/L) had a 60% increased risk of knee rOA. Those with *D. farinae*-specific sensitization (>0.35kU/L) had 2.0 times increased risk of knee sxOA in compared to those without sensitization. Population-attributable fractions of knee rOA caused by high total IgE and knee sxOA caused by *D. farinae*-specific sensitization were 9.8% and 15.3%, respectively.

Conclusions: Total IgE and *D. farinae*-specific IgE were significantly associated with OA in knees of Korean adults. High total IgE and *D. farinae*-specific sensitization were also associated with their OA.

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Introduction

Osteoarthritis (OA) is the most common type of arthritis involving destruction of cartilage matrix. It most commonly occurs in the knees, followed by that in the hand and hip^{1,2}. In 2011, a systematic review study showed that global prevalence of radiographic knee OA (rOA) of 45.1% and 33.4% and global prevalence of radiographically confirmed symptomatic knee OA (sxOA) of 15.7% and 8.8% in women and men, aged 60 years or more, respectively². Another systematic review study reported that a global prevalence of knee sxOA of 3.8% (4.8% in women and 2.8% in men) in 2010³. In 2017, there were 263.1 million all-age global prevalent cases of knee OA, and 12.9 million incident cases⁴. The global number of years

lived with disability (YLDs) for knee OA in 2017 was 8.3 million. Increase of YLDs for knee OA was as 63.7% between 1990 and 2007, and 30.8% between 2007 and 2017⁴. Because knee OA is expected to become a more common global condition with worldwide aging, more attention should be paid to identification of risk factors for knee OA.

Immunoglobulin E (IgE) is utilized during immune response against certain protozoan parasites. It plays a crucial role in responses to allergens. Increased IgE levels or IgE sensitizations is also associated with increased risks of some chronic diseases, such as asthma⁵, diabetes mellitus⁶, ischemic heart diseases⁷, age-related cataract⁸ and cancer⁹. The function of IgE is associated with its ability to activate mast cells. Thus, it may play critical roles in certain chronic diseases (e.g., diabetes mellitus)¹⁰. Although the role of IgE in other chronic diseases has been extensively studied, epidemiologic study that addresses the relationship between IgE and OA has not been reported yet.

In 2019, Wang *et al.* demonstrated that IgE/high-affinity IgE receptor (FcεRI)/spleen tyrosine kinase (Syk) signaling axis was

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important in the pathogenesis of OA. They concluded a central role for IgE-dependent mast cell activation in the development of OA¹¹. Therefore, we hypothesized that a high total IgE and allergen-specific IgE levels might be associated with increased risk of knee rOA and sxOA. Therefore, we tested this hypothesis using a nationally representative population survey data.

Method

This study used data acquired from the Korea National Health and Nutrition Examination Survey (KNHANES), 2010 (<https://knhanes.cdc.go.kr>). KNHANES is a cross-sectional investigation body that collects health and nutritional status of the national representative population in South Korea. For sampling, the Korean Centers for Disease Control and Prevention (KCDC) uses stratified and multistage probability cluster sampling approach. This survey collected data using health interview and examination with nutrition survey. Among the entire participants in KNHANES 2010 ($n = 10,938$), KCDC planned to investigate all participants aged 50 years or more for their OA status and only 2,400 participants aged 10 years or more for serum total IgE or allergen-specific IgE levels. All participants of KNHANES provided signed consent forms for their participation. KNHANES followed the Declaration of Helsinki recommendation on Ethical Principles for Medical Research Involving Human Subjects. This study was exempt from the ethical review by the institutional review board of the University of Seoul (exempt no. 2019-23). Of participants in KNHANES 2010, this study used data obtained from men and women participants aged 50 years old or more who were examined for OA in the knees and serum total IgE or allergen-specific IgE levels.

Risk factors of interest were total IgE and allergen-specific IgE levels. KNHANES examined the following specific IgE levels: *Der-matophagoides farinae*, cockroach, and dog allergens. All IgE levels were analyzed using a 1450 Wizard Gamma Counter (Perkin Elmer, Turku, Finland). Participants with total IgE levels >150 U/ml were defined as having high total IgE. Those with allergen-specific IgE levels >0.35 kU/L were defined as being sensitized.

Outcomes of interest were rOA and sxOA in the knees. The knees were radiographically examined for bilateral anteroposterior, weight-bearing anteroposterior and lateral plain (with 30° angle flexion) aspects by using a DigiRAD-PG 9M X-ray machine (SITEC Medical, Kimpo, South Korea). To assess rOA in the knees, KNHANES used Kellgren–Lawrence grading system¹². The degree of rOA in the knees was graded from 0 to 4, where 0 = absent abnormal finding, 1 = questionable osteophyte with normal joint space, 2 = definite osteophyte with possible joint space narrowing, 3 = definite osteophyte with moderate joint space narrowing, and 4 = severe joint space narrowing with subchondral sclerosis. The participants with Kellgren–Lawrence grade ≥ 2 in either knee was classified as having rOA in the knee. Radiographic digital images were shared with musculoskeletal radiologists. Two radiologists independently read these images. If radiologists have the same grade for status of each joint, the concordance grade of each joint was accepted. If two radiologists suggested one-grade difference, the higher grade was accepted. If they suggested discrepant grades greater than one-grade, a third radiologist resolved the issue. We determined sxOA by both the presence of rOA and OA symptoms. The OA symptoms were defined using a questionnaire. If the participant reported joint pain for more than 30 days during the past 3 months, he or she was defined as having OA symptom.

We used the following covariates collected from self-reported questionnaires and face-to-face interviews; age, sex, alcohol consumption, smoking amount, metabolic equivalence task (MET), education, occupation and income. We obtained data for the following covariates from health examination: serum 25-

hydroxyvitamin D (25(OH) D) levels, degree obesity and status of fasting blood glucose. KNHANES measured serum 25(OH)D levels using a radioimmunoassay kit (DiaSorin Inc., Stillwater, MN, USA) with a 1470 Wizard gamma counter (PerkinElmer, Turku, Finland). The degree of obesity was determined by using body mass index (BMI, kg/m²) which was estimated by dividing weight (kg) by squared height (m²). KNHANES measured the weight and height by using a calibrated balance-beam scale (GL-6000–20; G-tech, Seoul, Korea) and a stadiometer (SECA 225; SECA, Hamburg, Germany), respectively. We defined the normal weight, overweight, and obese as having BMI <23 kg/m², 23–24.9 kg/m², and ≥ 25 kg/m², respectively¹³. KNHANES collected blood samples from participants in the morning and analyzed those samples by using an auto-analyzer (Hitachi Automatic Analyzer model 7600; Hitachi, Tokyo, Japan). To determine the status of the fasting blood glucose, our study used data from participants who had 8-h overnight fasting status. We defined normal fasting glucose, impaired fasting glucose, and diabetes mellitus as having fasting glucose <100 mg/dL, 100–125.9 mg/dL, and ≥ 126 mg/dL, respectively.

For statistical analysis, the participants were grouped into tertiles according to their serum total IgE level (2.0–55.3, 55.4 to 220.0, and 221.0–5000.0 kU/L), *D. farinae*-specific IgE level (0.01–0.05, 0.06 to 0.39, and 0.40–100.01 kU/L), cockroach-specific IgE level (0.01–0.03, 0.04 to 0.15, and 0.16–29.9 kU/L), and dog-specific IgE level (0.01–0.01, 0.02 to 0.03, and 0.04–11.2 kU/L). We then examined relationships between the tertiles of IgE levels and OA by using multivariable logistic regression analyses. In each analysis, we sequentially adjusted the following variables: model 1 adjusted for age and sex; model 2 additionally for alcohol consumption, smoking amount, MET, income, 25(OH)D levels, education, and occupation; and model 3 additionally for degree of obesity and status of fasting blood glucose. We also examined relationships between continuous IgE levels and OA by using multivariable logistic regression analyses with the same adjustments for the three models. We then examined the relationship between the OA and total or allergen-specific sensitization. Lastly, we estimated population attributable fractions (PAFs) as measures of OA attributed to the total and allergen-specific sensitization after adjusting for variables in model 3 by using R version 3.4.3 - AF package (R Foundation for Statistical Computing). We did not perform correction for multiple testing because of the exploratory approach of this study to the relationship between IgE levels and allergic sensitizations and OA of knee. With the exception of PAFs, we performed all statistical analyses by using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was considered at P value < 0.05 .

Results

Out of 3273 participants with age ≥ 50 years in KNHANES 2010, we excluded those who were not examined for OA in the knee ($n = 198$) and those who had no information for serum total IgE or allergen-specific IgE level ($n = 2290$). Finally, our study population had composed of 785 participants. Prevalence of rOA and sxOA were 33.5% and 11.2%, respectively (Table I). The medians of total IgE and *D. farinae*-, cockroach-, and dog-specific IgE levels were 105 kU/L, 0.15 kU/L, 0.07 kU/L, and 0.02 kU/L, respectively.

After adjusting for all confounders, we found out that the participants with a high total IgE had 92% increased risk of rOA compared to those with low total IgE. A significant trend was found across tertiles (Table II). The participants with middle and high levels of total IgE had 90% and 242% increased risk of sxOA, respectively, compared to those with low total IgE. A significant trend was found across tertiles. Participants with high *D. farinae*-specific IgE had 2.2 times increased risk of sxOA

Variable	rOA		sxOA	
	Non-OA	OA	Non-OA	OA
n	522	263	690	87
Men, %	55.8	38.4	52.9	24.1
Age, yr	58.8 ± 6.2, 58.0	63.1 ± 6.8, 63.0	59.7 ± 6.5, 59.0	64.8 ± 6.9, 66.0
Lifestyle				
Alcohol consumption, g/d	67.2 ± 135.0, 4.2	49.3 ± 121.2, 1.8	63.8 ± 132.8, 3.6	34.8 ± 95.6, 1.8
Smoking amount, pack-years	13.7 ± 20.5, 0.0	9.2 ± 17.8, 0.0	13.0 ± 20.3, 0.0	5.9 ± 13.3, 0.0
MET, MET-min/wk	3174 ± 4549, 1680	3290 ± 4541, 1680	3224 ± 4602, 1680	3231 ± 4157, 1680
Socioeconomic status, %				
Education				
≤Middle school	56.8	71.7	58.9	85.1
High school	28.4	21.1	28.1	9.2
≥College	14.8	7.3	13.1	5.8
Occupation				
White collar	12.7	6.5	11.8	1.2
Blue collar	51.7	46.5	51.0	41.4
Unemployed/household	35.6	46.9	37.1	57.5
Income (≥2,000 US\$/mo)	62.1	46.3	60.1	34.9
Serum 25(OH)D levels, ng/mL	19.2 ± 6.9, 18.1	19.6 ± 7.1, 18.6	19.5 ± 7.0, 18.3	18.4 ± 6.9, 17.8
Degree of obesity, %				
Normal weight (<23 kg/m ²)	44.8	22.1	39.1	21.8
Overweight (23–24.9 kg/m ²)	25.7	27.0	26.8	21.8
Obese (≥25 kg/m ²)	29.5	51.0	34.1	56.3
Fasting blood glucose, %				
Normal (<100 mg/dL)	62.0	58.6	61.5	56.0
Impaired (100–125.9 mg/dL)	23.8	23.1	23.5	23.8
Diabetes mellitus (≥126 mg/dL)	14.3	18.4	15.1	20.2
Serum IgE levels, kU/L				
Total IgE	347.0 ± 729.1, 101.0	394.5 ± 810.6, 114.0	368.5 ± 783.4, 101.5	308.6 ± 493.6, 121.0
<i>D. farinae</i> -specific IgE	2.19 ± 8.83, 0.15	2.09 ± 8.07, 0.17	2.19 ± 8.80, 0.15	1.76 ± 6.88, 0.19
Cockroaches-specific IgE	0.51 ± 1.78, 0.07	0.45 ± 1.45, 0.07	0.52 ± 1.78, 0.07	0.21 ± 0.35, 0.06
Dog-specific IgE	0.13 ± 0.73, 0.02	0.13 ± 0.53, 0.02	0.13 ± 0.67, 0.02	0.12 ± 0.66, 0.02

Data are mean ± SD, median or %. *P* values were calculated by *t*-tests or Chi-square tests.

Table I Basic characteristics of study participants

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compared to those with low *D. farinae*-specific IgE. A significant trend was found across tertiles.

The risk OA increased significantly with increasing total and *D. farinae*-specific IgE as continuous variables (Table III). For those with an exponential increase in total IgE, risks of rOA and sxOA increased by 44% and 53%, respectively. The risk of sxOA increased by 40% for those with an exponential increase in *D. farinae*-specific IgE. Participants with high total IgE had 60% increased risk of rOA. Those with *D. farinae*-specific sensitization had 2.0 times increased risk of sxOA, compared to those without sensitization (Table IV). PAFs of rOA caused by high total IgE and PAFs of sxOA caused by *D. farinae*-specific sensitization were 9.8% [95% confidence interval (CI) = 2.1–17.5%, *P* value = 0.013] and 15.3% (95% CI = 2.7–27.9%, *P* value = 0.018), respectively. These results showed that 9.8% of rOA was attributable to high total IgE and 15.3% of sxOA was attributable to *D. farinae*-specific sensitization in our study population. However, we could not find any other significant PAFs of OA caused by IgE sensitizations.

Discussion

Our study showed that increased total and *D. farinae*-specific IgE levels were significantly associated with increased risks of OA in the knees. We also found a significant linear relationship between total or *D. farinae*-specific IgE and odds of OA. High total IgE and

D. farinae-specific sensitizations were also significantly associated with increased risks of OA in the knees. PAF estimates indicated that 9.8% of sxOA could be eliminated after removing high total IgE and 15.3% of rOA could be eliminated after removing *D. farinae*-specific sensitizations. Therefore, our findings suggest that old adults who have increased IgE levels should be monitored for OA in the knees.

It is difficult to suggest potential mechanisms of the relationship between serum IgE levels and knee OA because few studies have investigated the issue. One of the most plausible explanations is that a variety of stimuli such as allergens can cross-link IgE-bound FcεRI and lead mast cell degranulation and activation, thus mediating inflammation and tissue damage in the development of OA through mast cell-derived tryptase, at least in part¹¹. Therefore, IgE was significantly associated with OA as an indicator of the IgE/FcεRI/Syk signaling axis. A recent study has shown that anti-IgE treatment can improve pain and disability of patients with knee OA and atopic disease¹⁴, supporting the contribution of mast cells to OA.

Our study showed that the total and *D. farinae*-specific IgE levels were associated with sxOA. Pain is a common and the most disabling symptom for patients with OA¹. Neuropathic pain of OA is produced by nerve changes in the spinal cord or peripheral nervous system or from structural changes in joint innervation¹⁵. Inhibition of descending antinociceptive pathways and activation of

	Tertiles of serum IgE levels			P for trend
	T1	T2	T3	
Total IgE, kU/L	2.0–55.3 (<i>n</i> = 261)	55.4–220.0 (<i>n</i> = 262)	221.0–5000.0 (<i>n</i> = 262)	
Mean ± SD, median	25.8 ± 15.1, 24.8	111.1 ± 42.8, 104.5	950.6 ± 1094, 514.5	
rOA				
Model 1	Reference	1.35 (0.90–2.01), 0.14	1.91 (1.25–2.94), 0.003	0.003
Model 2	Reference	1.33 (0.88–2.01), 0.17	1.86 (1.19–2.90), 0.006	0.006
Model 3	Reference	1.31 (0.86–2.01), 0.21	1.92 (1.21–3.04), 0.006	0.006
sxOA				
Model 1	Reference	1.75 (0.96–3.17), 0.07	2.63 (1.37–5.02), 0.004	0.003
Model 2	Reference	1.90 (1.03–3.52), 0.041	2.61 (1.33–5.12), 0.005	0.005
Model 3	Reference	1.90 (1.00–3.60), 0.049	2.42 (1.19–4.90), 0.014	0.012
<i>D. farinae</i> -specific IgE, kU/L	0.01–0.05 (<i>n</i> = 265)	0.06–0.39 (<i>n</i> = 258)	0.40–100.01 (<i>n</i> = 261)	
Mean ± SD, median	0.02 ± 0.01, 0.02	0.17 ± 0.09, 0.16	6.28 ± 14.01, 1.69	
rOA				
Model 1	Reference	1.17 (0.79–1.73), 0.44	1.39 (0.92–2.09), 0.12	0.12
Model 2	Reference	1.14 (0.76–1.71), 0.53	1.31 (0.84–2.02), 0.23	0.23
Model 3	Reference	1.17 (0.77–1.79), 0.46	1.31 (0.83–2.06), 0.25	0.25
sxOA				
Model 1	Reference	1.36 (0.75–2.45), 0.31	2.09 (1.13–3.88), 0.019	0.020
Model 2	Reference	1.24 (0.67–2.28), 0.49	2.15 (1.12–4.16), 0.022	0.025
Model 3	Reference	1.36 (0.72–2.57), 0.34	2.15 (1.08–4.30), 0.030	0.031
Cockroaches-specific IgE, kU/L	0.01–0.03 (<i>n</i> = 237)	0.04–0.15 (<i>n</i> = 287)	0.16–29.9 (<i>n</i> = 260)	
Mean ± SD, median	0.02 ± 0.01, 0.02	0.07 ± 0.03, 0.06	1.37 ± 2.71, 0.51	
rOA				
Model 1	Reference	1.32 (0.89–1.96), 0.17	1.33 (0.87–2.01), 0.19	0.19
Model 2	Reference	1.28 (0.85–1.92), 0.24	1.26 (0.81–1.94), 0.30	0.31
Model 3	Reference	1.32 (0.86–2.02), 0.20	1.20 (0.77–1.88), 0.42	0.43
sxOA				
Model 1	Reference	1.70 (0.96–3.04), 0.07	1.20 (0.63–2.27), 0.58	0.55
Model 2	Reference	1.59 (0.87–2.88), 0.13	1.18 (0.61–2.28), 0.63	0.60
Model 3	Reference	1.57 (0.85–2.89), 0.15	1.06 (0.53–2.12), 0.87	0.82
Dog-specific IgE, kU/L	0.01–0.01 (<i>n</i> = 287)	0.02–0.03 (<i>n</i> = 221)	0.04–11.2 (<i>n</i> = 275)	
Mean ± SD, median	0.01 ± 0.00, 0.01	0.02 ± 0.00, 0.02	0.35 ± 1.09, 0.10	
rOA				
Model 1	Reference	1.07 (0.71–1.60), 0.75	1.28 (0.87–1.89), 0.21	0.21
Model 2	Reference	1.10 (0.72–1.67), 0.66	1.26 (0.84–1.89), 0.27	0.27
Model 3	Reference	1.15 (0.74–1.77), 0.54	1.24 (0.81–1.89), 0.33	0.32
sxOA				
Model 1	Reference	1.56 (0.87–2.80), 0.14	1.29 (0.71–2.32), 0.40	0.36
Model 2	Reference	1.55 (0.84–2.85), 0.16	1.31 (0.71–2.43), 0.39	0.35
Model 3	Reference	1.62 (0.86–3.06), 0.14	1.23 (0.65–2.34), 0.52	0.47

Boldface indicates a *P* value < 0.05. Model 1 adjusted for age and sex. Model 2 adjusted for variables in model 1, alcohol consumption, smoking amount, MET, income, 25(OH)D levels, education, and occupation. Model 3 adjusted for variables in model 2, degree of obesity, and status of fasting blood glucose.

Table II OR (95% CI) of knee OA according to tertiles of serum IgE levels

descending pain facilitation pathways are mechanisms underlying central pain¹⁶. Indeed, a systematic review study has shown that 23% of patients with hip or knee OA have neuropathic pain.¹⁷

Among allergens, only *D. farinae*-specific IgE level or sensitization was significantly associated with knee OA. The highest partial correlation of total IgE levels with *D. farinae*-specific IgE levels (Pearson $r = 0.52$, P value < 0.001) compared to other allergen-specific IgE levels ($r = 0.15$ – 0.32 , P values < 0.001) might have induced this phenomenon. High correlation was also found in the relationship between high total IgE and *D. farinae*-specific IgE sensitization (Phi coefficient = 0.59, P values < 0.001). Moreover, *D. farinae*-specific IgE levels and sensitization were significantly associated with only sxOA of the knee. Since the magnitude of the relationship between *D. farinae*-specific IgE and knee OA was not large compared to total IgE, more severe outcome, sxOA, appeared to have a significant relationship with *D. farinae*-specific IgE.

However, possible biological mechanisms for these are currently unclear. Future studies are needed to elucidate mechanisms of the close relationship between *D. farinae*-specific IgE and knee OA.

To our knowledge, this is the first study to address the relationship between IgE levels and OA. Another strength of this study was that we used data acquired from nationally representative population to assess our hypothesis. However, our study also has some limitations. First, we only found the association between IgE levels and knee OA because our study analyzed the cross-sectional KNHANES data. For example, increased IgE levels and OA might be attributed to a third cause simultaneously. Second, we should be cautious when generalizing our study results to population that has different genetic factors, lifestyles, and cultural environments.

In conclusion, our findings indicate that IgE levels are significantly associated with OA in the knees of old adults. Significant proportions of patients having OA in the knee can be eliminated by

Risk factor	Outcome	Model 1	Model 2	Model 3
Total IgE, kU/L	rOA	1.45 (1.12–1.88), 0.004	1.47 (1.12–1.92), 0.005	1.44 (1.09–1.91), 0.010
	sxOA	1.55 (1.06–2.28), 0.024	1.62 (1.08–2.43), 0.019	1.53 (1.00–2.33), 0.048
<i>D farinae</i> -specific IgE, kU/L	rOA	1.17 (0.98–1.40), 0.08	1.18 (0.97–1.43), 0.10	1.15 (0.94–1.41), 0.16
	sxOA	1.36 (1.04–1.78), 0.025	1.42 (1.05–1.91), 0.021	1.40 (1.03–1.92), 0.034
Cockroaches-specific IgE, kU/L	rOA	1.14 (0.89–1.46), 0.28	1.11 (0.86–1.43), 0.42	1.05 (0.81–1.37), 0.70
	sxOA	1.00 (0.68–1.46), 0.98	0.99 (0.66–1.48), 0.96	0.91 (0.60–1.38), 0.65
Dog-specific IgE, kU/L	rOA	1.29 (0.96–1.74), 0.09	1.27 (0.92–1.75), 0.15	1.20 (0.85–1.68), 0.29
	sxOA	1.14 (0.71–1.82), 0.59	1.20 (0.72–1.99), 0.48	1.02 (0.60–1.75), 0.93

Boldface indicates a *P* value < 0.05. Model 1 adjusted for age and sex. Model 2 adjusted for variables in model 1, alcohol consumption, smoking amount, MET, income, 25(OH)D levels, education, and occupation. Model 3 adjusted for variables in model 2, degree of obesity, and status of fasting blood glucose. Risk factors were naturally log-transformed.

Table III Relationships between serum IgE levels and knee OA

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Risk factor	Outcome	Model 1	Model 2	Model 3
Total IgE >150 kU/L	rOA	1.59 (1.12–2.25), 0.010	1.54 (1.07–2.22), 0.020	1.60 (1.09–2.34), 0.016
	sxOA	1.74 (1.03–2.92), 0.037	1.76 (1.02–3.04), 0.043	1.74 (0.98–3.08), 0.06
<i>D farinae</i> -specific IgE >0.35 kU/L	rOA	1.38 (0.97–1.96), 0.07	1.33 (0.92–1.93), 0.13	1.32 (0.90–1.94), 0.16
	sxOA	1.94 (1.15–3.28), 0.014	2.09 (1.19–3.68), 0.010	2.02 (1.12–3.66), 0.020
Cockroaches-specific IgE >0.35 kU/L	rOA	1.12 (0.75–1.68), 0.58	1.08 (0.71–1.65), 0.73	0.98 (0.63–1.52), 0.93
	sxOA	1.12 (0.59–2.12), 0.72	1.11 (0.57–2.13), 0.76	1.01 (0.51–2.00), 0.99
Dog-specific IgE >0.35 kU/L	rOA	1.91 (0.94–3.88), 0.07	1.67 (0.77–3.60), 0.19	1.50 (0.67–3.37), 0.33
	sxOA	0.58 (0.13–2.56), 0.48	0.73 (0.16–3.34), 0.69	0.34 (0.04–2.67), 0.30

Boldface indicates a *P* value < 0.05. Model 1 adjusted for age and sex. Model 2 adjusted for variables in model 1, alcohol consumption, smoking amount, MET, income, 25(OH)D levels, education, and occupation. Model 3 adjusted for variables in model 2, degree of obesity, and status of fasting blood glucose.

Table IV Relationships between serum allergic sensitization and knee OA

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controlling serum IgE levels. Future prospective studies should be performed to confirm the effect of IgE level on OA.

Author contributions

S Park designed the study, analyzed and interpreted data, and drafted the manuscript. N Choi designed the study and drafted the manuscript. All authors contributed to the writing of the final manuscript.

Conflict of interest

All authors declared no conflict of interest.

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