Dyslipidemia is Associated with an Increased Risk of Knee Osteoarthritis Regardless of Obesity: An Analysis of a Nationwide South Korean Cohort

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INTRODUCTION: Characterized by the degradation of cartilage, joint pain, and restricted range of motion, knee osteoarthritis (OA) significantly deteriorates the quality of life for those affected. While traditional risk factors such as age, obesity, malalignment, and excessive mechanical stress have been well-established, there is emerging evidence that metabolic factors may also be implicated in the onset and progression of OA. Metabolic syndrome encompasses a range of risk factors, including diabetes, obesity, dyslipidemia, and hypertension. While obesity has been linked to degenerative joint changes due to excessive mechanical load, the occurrence of OA in non-weight-bearing joints such as the hand suggests that metabolic elements like adipokines, for example leptin, may also play a role. This raises the possibility that OA could have a systemic metabolic component. However, the relationship between dyslipidemia and knee OA remains inadequately understood within a broad epidemiological context. The hypothesis was that individuals with dyslipidemia may have a higher incidence of knee OA. To test this hypothesis, this study aimed 1) to investigate the association between dyslipidemia and the incidence of knee OA and 2) to compare the incidence of knee OA according to body mass index (BMI) in a nationwide South Korean cohort.

METHODS: This nationwide retrospective cohort study leverages the extensive National Health Insurance Service (NHIS) database to investigate the association between knee OA and dyslipidemia in South Korea. Employing a case-control design, the study divided 744,879 participants into OA and non-OA groups. The OA group consisted of individuals aged 18 and above, diagnosed with knee OA in 2020 according to ICD code M17. The non-OA group comprised individuals who did not receive an osteoarthritis diagnosis in 2020 and were age- and sex-matched with patients in the OA group. Propensity score matching was utilized to adjust for confounding factors like age, sex, and comorbidities (diabetes, hypertension, and osteoporosis). Both univariate and multivariate logistic regression models were applied to analyze baseline characteristics and assess odds ratios (ORs) for knee OA incidence in various dyslipidemia subcategories.

RESULTS: The prevalence of dyslipidemia was statistically significantly higher in the OA group compared to the non-OA group (66.2% in the OA group versus 60.7% in the non-OA group, Table 1). Utilizing a univariate logistic regression model, significant differences were observed for age, sex, BMI, smoking status, dyslipidemia, and comorbidities. Further analysis using a multivariate logistic regression model revealed that the likelihood of receiving an OA diagnosis was associated with having a BMI greater than 23 kg/m² (OR 1.035; 95% CI 1.024-1.045), being a former smoker (OR 1.038; 95% CI 1.021-1.054), having dyslipidemia (OR 1.290; 95% CI 1.275-1.305), and receiving an osteoporosis diagnosis (OR 1.112; 95% CI 1.097-1.128, Table 2). In subgroups of patients with a BMI above and below 30, multivariate logistic regression analysis revealed an increased odds ratio for the diagnosis of osteoarthritis when dyslipidemia was present. However, no significant difference was observed between the two subgroups.

DISCUSSION: This study demonstrated that the risk of OA was obviously higher among those suffering from dyslipidemia compared to those without dyslipidemia even after adjusting for other risk factors like age, sex, and BMI. Further in vitro or in vivo studies are needed to elucidate the pathophysiological mechanisms by which lipid profiles may influence the development of knee OA. Additionally, more research is warranted to determine whether the regulation of dyslipidemia could contribute to OA treatment.

Significance/Clinical Relevance: Based on the findings of this study, new insights into the potential metabolic conditions affecting knee OA could be gained, thereby informing enhanced diagnostic, preventive, and therapeutic strategies for this debilitating condition.

Table 1. Baseline characteristics of study population according to incident OA

	Total (n=744,879)	Non-OA (n=496,586)	OA (n=248,293)
Age (years)	55.04±11.23	54.94±11.03	55.23±11.60
Sex			
Male	364502 (48.93%)	245508 (49.44%)	118994 (47.92%)
Female	380377 (51.07%)	251078 (50.56%)	129299 (52.08%)
BMI (kg/m^2)	23.61±3.27	23.55±3.24	23.74±3.31
Smoking status			
Never smoked	471143 (63.25%)	313077 (63.05%)	158066 (63.66%)
Former smoker	130042 (17.46%)	86949 (17.51%)	43093 (17.36%)
Current smoker	143694 (19.29%)	96560 (19.44%)	47134 (18.98%)
Dyslipidemia			
No	279374 (37.51%)	195357 (39.34%)	84017 (33.84%)
Yes	465505 (62.49%)	301229 (60.66%)	164276 (66.16%)
Comorbidities (Yes)			
Hypertension	227756 (30.58%)	150135 (30.23%)	77621 (31.26%)
Diabetes	235142 (31.57%)	154813 (31.18%)	80329 (32.35%)
Osteoporosis	127910 (17.17%)	81560 (16.42%)	46350 (18.67%)

OA, osteoarthritis; BMI, body mass index

Table 2. Multivariate logistic regression analysis for OA incidence

Variables	OR (95% CI)	P-value
Age	0.999 (0.999-1.000)	0.037
Sex		
Female (vs. male)	1.060 (1.046-1.074)	<0.001
BMI ≥23 kg/m^2		
Yes (vs. no)	1.035 (1.024-1.045)	<0.001
Smoking status		
Never smoked	Reference	
Former smoker	1.038 (1.021-1.054)	<0.001
Current smoker	1.016 (1.000-1.031)	0.048
Dyslipidemia		
Yes (vs. no)	1.290 (1.275-1.305)	<0.001
Comorbidities		
Osteoporosis	1.112 (1.097-1.128)	<0.001

OR, Odds ratio; CI, confidence interval