



The prevalence of type 2 diabetes and associated risk factors with generalized osteoarthritis: a retrospective study using ICD codes for clinical data repository system

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Abstract

Objective Type 2 diabetes mellitus (T2DM) has been associated with osteoarthritis (OA). T2DM may be associated with generalized OA (GOA ≥ 3 joints) rather than localized OA (LOA < 3 joints). The purpose of this study was to examine the prevalence of T2DM in people with GOA compared with LOA and to investigate the association between demographic risk factors and chronic diseases (i.e., T2DM, hypertension, dyslipidemia, neuropathy, and body mass index (BMI)) with GOA compared with LOA.

Methods A retrospective review of data was performed, and patients with diagnostic codes for OA were selected. Identified codes included primary GOA, primary LOA, T2DM, hypertension, dyslipidemia, neuropathy, depression, anxiety, and sleep disorders. Information about BMI and medication list was obtained. Chi-square and logistic regression were performed to examine the prevalence and risk factors, respectively.

Results Data from 3855 patients (mean age = 66.43 ± 11.02 , 60.9% women) included patients with GOA ($n = 1265$) and LOA ($n = 2590$). The prevalence of T2DM was significantly greater among patients with GOA (25.8%) compared with those with LOA (12.0%); however, the GOA group were older. Based on age groups, T2DM was prevalent in 17.8% of GOA compared with 7.2% in LOA for younger adults (aged 45–64 years) and was prevalent in 28.8% of GOA compared with 15.7% in LOA for older adults (aged 65 years or older). The odds ratio of GOA increased in people with chronic diseases compared with those without including T2DM (odds ratio (OR) 1.37, 95% confidence interval (CI) 1.05–1.78, $p = 0.02$), hypertension (OR 1.99, CI 1.63–2.43, $p < 0.001$), and dyslipidemia (OR 3.46, CI 2.86–4.19, $p < 0.001$), adjusting for covariates.

Conclusion Higher prevalence of T2DM was found in people with GOA when compared with LOA across both age groups. T2DM, hypertension, and dyslipidemia were associated with GOA. Future research with longitudinal designs is needed to test the causality of this association.

Key Points

- The prevalence of type 2 diabetes in people with generalized osteoarthritis was almost double compared with localized osteoarthritis, although generalized osteoarthritis group were older.
- Among people with osteoarthritis, the risk of generalized osteoarthritis is increased by 37% when people had type 2 diabetes, by 99% when people had hypertension, and by 246% when people had dyslipidemia.

Keywords Diabetes · Dyslipidemia · High blood pressure · Multisite osteoarthritis

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Introduction

Osteoarthritis (OA) and type 2 diabetes mellitus (T2DM) are common chronic diseases affecting 15% and 8.5% worldwide, respectively [1, 2]. OA is characterized by joint degeneration and inflammation, and it may be classified as either localized or generalized OA depending on the number of joints affected. Generalized OA (GOA) affects 3 or more joints and localized OA affects less than 3 joints [3]. Previous evidence with a small sample found that GOA affects 50% of people with knee OA [4]. People with GOA may present with worse symptoms or outcomes in terms of pain, functionality, and quality of life [5].

T2DM results in chronic hyperglycemia, which may affect the musculoskeletal system. Hyperglycemia may induce chronic systemic inflammation that leads to systemic changes that may affect joints through the remodeling of collagen types in cartilage and synovia [6]. Another consequence of hyperglycemia is the production of advanced glycation end products (AGE) that may increase cartilage stiffness and bone fragility [7]. In addition to OA risk in people with T2DM, a recent report highlighted the lack of comprehensive risk factor assessment or treatment in the USA. This study reported that only 1 in 5 persons with T2DM achieve comprehensive risk factor control such as blood pressure, glycemic control, and lipid profile [8].

Diabetes and OA are common diseases that are associated with common risk factors and complications. Although a few studies have highlighted the association between diabetes and OA [9–16], others have found no association [17–20]. Inconsistent findings could be partially explained by small sample sizes [12] and a primary focus on weight-bearing joints such as the knees [9, 10, 15, 16] or on a specific single body part such as the hands [17, 18]. Definitions for OA were inconsistent across studies as one study defined OA as arthroplasty in hip or knee joint [14]. Other factors such as age, ethnicity, sex, body mass index (BMI), hypertension, neuropathy, and dyslipidemia, which impact both diabetes and OA, have not been fully examined or controlled for in previous analyses [9–16]. Although neuropathy is a common complication of diabetes, it has not been studied as a risk factor for OA. Previous studies have shown that women have a higher prevalence of hip and knee OA than men [21]. Race has been shown to be associated with OA in non-Hispanic African Americans [22]. Older age has been associated with LOA (e.g., knee, hip or hand) [19, 21]. However, whether other factors are associated with GOA versus LOA is still unclear. Understanding the association between these risk factors and GOA may enhance our knowledge about this understudied population with GOA as the treatment approach is different for each condition (GOA vs. LOA).

Previous reports have found associations between other metabolic syndromes (e.g., dyslipidemia, hypertension, or

obesity) and OA [15, 23]. However, the research is also hampered by the limited sites for OA, a focus on LOA (hand or knee OA) [15, 23], and/or lack of control for other risk factors such as T2DM, hypertension, and dyslipidemia within the same model [15, 23]. Because some medications such as antihypertensive and antilipemic could affect the OA progression and symptoms [24, 25], the use of medications should also be adjusted in the analyses.

People with generalized OA may benefit more from systemic and interdisciplinary approaches than people with single joint OA [26]. The association between T2DM and OA has been investigated, but the association with which type of OA such as GOA versus LOA is still unknown. Examining the prevalence of T2DM and associated risk factors with GOA is crucial because of the high prevalence of GOA among the overall OA population with worse outcomes, and GOA might be a marker of more severe disease with increased progression [5]. Therefore, the objectives of this study were (1) to examine the prevalence of T2DM among patients with GOA compared with the prevalence of T2DM in patients with LOA, and (2) to investigate the association between demographic risk factors (age, gender, and race) and chronic disease risk factors (T2DM, hypertension, dyslipidemia, neuropathy, and BMI) with GOA compared with LOA.

Materials and methods

Design and setting

This study is a retrospective analysis of de-identified data using the Healthcare Enterprise Repository for Ontological Narration (HERON) [27]. This database provides researchers access to de-identified electronic medical records from a tertiary hospital or its affiliated clinics using Epic EMR. HERON includes data from other administrative, research, and public sources such as the clinics' billing system (GE IDX), the University Health System Consortium, tumor registries, and the death index from the Social Security Administration. The data warehouse contains demographic data (age, sex, and race), service use, clinical data (diagnoses codes, flowsheet, laboratory, and patients' vitals), and pharmacy data. As this data is de-identified, the study received an exempt determination from the institutional review board. Consent form from patients was not required by the HERON database after removing the identified data since the resulting data is deemed non-human subjects research by the institute. Therefore, an approval from the Data Request Oversight Committee was obtained for this analysis.

The study participants were selected using the i2b2 query and analysis tool [28] of the HERON database [27]. Patients 45 years old and older who were seen between 2011 and 2017 were selected if they had at least two diagnosis codes of

osteoarthritis separated by at least 1 day using either International Classification of Disease 9th revision (ICD-9) or International Classification of Disease 10th revision (ICD-10). Osteoarthritis diagnosis was categorized as either GOA or LOA based on ICD-9 or ICD-10 codes. GOA cohort and LOA cohort were extracted separately. For example, a query was built for GOA cohort only to include patients with only GOA and exclude LOA and vice versa to ensure accuracy of categorizing each cohort and minimizing the likelihood of having different codes for the same patient (GOA and LOA). The first OA diagnosis code was set as the index date followed by a second similar diagnosis between 2011 and 2017. Previous research has validated using ICD codes against chart review, self-reported OA, American College of Rheumatology criteria, or joint radiographs with good specificity and accuracy [29, 30]. Patients were excluded if they had at least one specific ICD-9 or ICD-10 codes for type 1 diabetes, fibromyalgia, secondary OA, neoplasm, gout, systemic lupus, arthritis with infection, rheumatoid arthritis, trigeminal nerve disorders, or carpal tunnel syndrome.

Variables and covariates

Demographic data included age, sex (males or females) and race (Caucasian, African American, or other). Data for chronic diseases (type 2 diabetes, hypertension, dyslipidemia, and neuropathy) was selected based on at least two diagnoses codes separated by at least 1 day using ICD-9 or ICD-10. Body mass index (BMI) was obtained within 1 year before or after the index date (first OA diagnosis) due to the lack of BMI data at the index date. Covariates of depression, anxiety, or sleep disorder were included if there were at least two diagnoses codes separated by 1 day using ICD-9 or ICD-10, as these factors have been shown to be associated with OA [31–33]. List of medications was included within ± 90 days of the index date. For each participant, pharmacy data was obtained and searched for the following medication types: pain medications (opioids, non-opioids, and benzodiazepine),

antidiabetics (insulin or hypoglycemic), antihypertensives, antilipemic, and antidepressants. The use of medication for each type was categorized as yes or no. Table 1 shows ICD-9 and ICD-10 codes for all variables of interest.

Statistical analyses

Descriptive results included frequencies and percentages for categorical variables or mean and standard deviation for continuous variables. Differences between groups were analyzed using the Fisher exact test for categorical variables or independent *t* test for continuous variables.

To examine the prevalence of T2DM among patients with OA, chi-square statistics were utilized based on two age groups including younger adults (45–64 years) and older adults (65 or older). To examine the individual contribution of OA category (GOA vs. LOA) and DM status (yes vs. no) based on age groups, we used individual chi-square tests for each cell in the contingency table and the associated standardized residuals (*R*). *R* can be calculated by this formula: $R = \frac{\text{observed cases } (O) - \text{expected cases } (E)}{\sqrt{E}}$, as utilized by Haberman [34] to test the deviation from the expected values separately for each cell. In other words, *R* indicates the difference between observed and expected cases and the standard deviation of the expected cases. *R* is considered when the strength of the measure between observed and expected cases needs to be tested to indicate which specific cell is significant the most and the least. Residuals greater than 2 indicated that observed cases were greater than the expected frequency or less than -2 indicated that observed cases were less than the expected frequency and were considered significantly different and selected as cutoffs [34].

Logistic regression analyses were used to examine the association between demographic factors (age, sex, and race) and chronic diseases (T2DM, hypertension, dyslipidemia, neuropathy, and BMI) with OA categories (GOA vs. LOA). Reference category for the outcome was set as LOA. Results

Table 1 Clinical diagnostic codes using ICD-9 and ICD-10

	ICD-9 codes	ICD-10 codes
Localized OA	715.1 (<i>N</i> = 15)	M16 (<i>n</i> = 314), M17 (<i>n</i> = 1186), M18 (<i>n</i> = 55), M19 (<i>n</i> = 1020)
Generalized OA	715.00	M15.xx
T2DM	250.xx	E11
Hypertension	401.xx	I10
Dyslipidemia	272.xx	E78
Neuropathy	356.9, 356.8, 357.2, 356.2, 356.0, 356.4, 250.6	E11.40, E11.41, E11.42, E11.43, G60
Depression	296.2, 296.3	F32, F33
Anxiety	300.00, 300.02	F41.1, F41.8, F41.9
Sleep disorders	307.4, 347.xx, 780.5	F51, G47.00, G47.1, G47.30

were presented in terms of calculated odds ratios (ORs) with 95% confidence intervals (95% CIs) for risk factors. Three models were created: (1) unadjusted bivariate model for each demographic and chronic disease factors; (2) adjusted for demographic factors (age, sex, and race); and (3) the primary analysis adjusted for all covariates (depression, anxiety, sleep disorders, medications (antidiabetics, antihypertensives, antilipemic, and antidepressants)) [24, 31, 33, 35–37] and each risk factors (age, sex, race, T2DM, hypertension, dyslipidemia, neuropathy, and BMI).

Because excluding cases may affect the results and create bias [38], missing values for BMI ($n = 1237$, 32.1%) were imputed using a multiple imputations method. The imputation model included age, sex, race, chronic diseases (T2DM, hypertension, dyslipidemia, neuropathy, depression, anxiety, and sleep disorders), and medications (antidiabetics, antihypertensives, antilipemic, and antidepressants). Imputation created five complete datasets according to Rubin's method [39]. The pooled results were used for data analysis. We conducted a sensitivity analysis comparing the results from the imputed data with the original dataset, and the results were similar. Therefore, we chose to report the multivariable results based on the imputed model. All statistical analyses were performed using SPSS 25 for mac (Chicago, IL). All analyses were conducted at the 0.05 alpha level.

Results

A total of 3855 patients were included in the analyses, of whom 639 (16.6%) had type 2 diabetes. Table 2 shows the characteristics of the full sample and GOA and LOA subsamples. There were statistically significant differences between people with GOA ($n = 1256$) and LOA ($n = 2590$) in terms of age, sex, race, chronic diseases including diabetes, hypertension, dyslipidemia, neuropathy, depression, anxiety, and sleep disorders. Data for BMI were available for 2088 (80.61%) participants with LOA and 530 (41.90%) participants with GOA.

For the prevalence of T2DM and GOA, Table 3 shows the results from chi-square statistics and standardized residuals. T2DM was significantly higher in people with GOA ($n = 327$, 25.8%) compared with LOA ($n = 312$, 12.0%).

However, GOA subsample was older than LOA. Standardized residuals for the overall prevalence of T2DM in people with GOA were 8.1. This standardized residual exceeded 2, indicating that the number of cases in the group of T2DM and GOA was significantly greater than what would be expected. Standardized residuals for the overall prevalence of T2DM in people with LOA were -5.7 , indicating that the number of cases in the group of T2DM and LOA was significantly smaller than what would be expected. The prevalence of T2DM based on age groups is presented in Table 3 as

follow: 17.8% in people with GOA vs. 7.2% in people with LOA in younger adults group (45–64 years) and 28.8% in people with GOA vs. 15.7% in people with LOA in older adults group (65 years or older). Standardized residuals for T2DM in people with GOA and LOA was greater than 2 and less than 2 in both age groups, respectively, indicating similar results to the overall prevalence.

Results from both unadjusted and adjusted logistic regression models are shown in Table 4. Demographic factors of age (OR 1.07, 95% CI 1.06–1.08) and gender (OR 2.04, 95% CI 1.77–2.36) increased the odds of having GOA. The odds ratios of having GOA increased for patients who had chronic diseases including T2DM, hypertension, dyslipidemia, or neuropathy than those who did not have chronic diseases after controlling for demographic factors.

Multivariable logistic regression results for the primary analysis are presented in Table 5. The odds ratio of GOA for patients with type 2 diabetes, hypertension, and dyslipidemia increased compared with those without after controlling for age, gender, race, depression, anxiety, sleep disorders, medications (antidiabetics, antihypertensives, antilipemic, and antidepressants), and other risk factors (T2DM, hypertension, dyslipidemia, neuropathy, and body mass index).

The results of sensitivity analysis for included patients ($n = 2618$) who had BMI without imputation showed similar significant results when compared with patients with imputation for BMI ($n = 3855$). The multivariable logistic regression for the primary sensitivity analysis indicated that odds of GOA was significantly increased in people with T2DM (OR 1.46, 95% CI 1.03–2.08, $p = 0.03$), hypertension (OR 1.91, CI 1.46–2.49, $p < 0.001$), and dyslipidemia (OR 2.91, CI 2.24–3.79, $p < 0.001$), after adjusting for covariates.

Discussion

This study examined the prevalence of T2DM in people with OA and investigated the risk factors (T2DM, hypertension, dyslipidemia, and neuropathy) associated with GOA. Our findings highlight the importance of screening for these risk factors, as previous research has found that only 1 in 5 persons with T2DM achieves comprehensive risk factor control, involving blood pressure, glycemic control, and lipid profile [8]. We observed a higher prevalence of T2DM in people with GOA (25.8%) when compared with LOA (12.0%) but patients in the GOA subsample were older. However, the prevalence according to each age group showed consistent results indicating that T2DM was more prevalent in people with GOA versus LOA. The overall prevalence of T2DM among patients with OA (either GOA or LOA) in the current study was 16.6%. This overall prevalence is consistent with the prevalence of diabetes among people with OA in a recent meta-analysis (14.4%) [40]. However, this study did not report the

Table 2 Participants' characteristics

	Total sample <i>N</i> = 3855	Generalized OA <i>N</i> = 1265	Localized OA <i>N</i> = 2590	<i>p</i> value
Age, years (mean ± SD)	66.43 ± 11.02	71.63 ± 10.55	63.90 ± 10.32	< 0.001
Sex, female, <i>n</i> (%)	2384 (60.9)	909 (71.9)	1439 (55.6)	< 0.001
Race, <i>n</i> (%)				< 0.001
Caucasians	3016 (78.2)	955 (75.5)	2061 (79.6)	
African American	500 (13)	222 (17.5)	278 (10.7)	
Others	339 (8.8)	88 (7.0)	251 (9.7)	
Body mass index (mean ± SE)	31.08 ± 7.10	30.50 ± 0.15	31.36 ± 0.35	0.04
Type 2 diabetes, <i>n</i> (%)	639 (16.6)	327 (25.8)	312 (12.0)	< 0.001
Hypertension, <i>n</i> (%)	1769 (45.9)	898 (71.0)	871 (33.6)	< 0.001
Dyslipidemia, <i>n</i> (%)	1442 (37.4)	839 (66.3)	603 (23.3)	< 0.001
Neuropathy, <i>n</i> (%)	172 (4.5)	99 (7.8)	73 (2.8)	< 0.001
Depression, <i>n</i> (%)	490 (12.7)	284 (22.5)	206 (8.0)	< 0.001
Anxiety, <i>n</i> (%)	441 (11.4)	275 (21.7)	166 (6.4)	< 0.001
Sleep disorders, <i>n</i> (%)	405 (10.5)	285 (22.5)	120 (4.6)	< 0.001
Medications				
Insulin, <i>n</i> (%)	164 (4.3)	38 (3.0)	126 (4.9)	0.007
Hypoglycemic, <i>n</i> (%)	326 (8.5)	48 (3.8)	278 (10.7)	< 0.001
Antihypertensive, <i>n</i> (%)	444 (11.5)	70 (5.5)	374 (14.4)	< 0.001
Antilipemic, <i>n</i> (%)	1046 (27.1)	164 (13.0)	882 (34.1)	< 0.001
Antidepressants, <i>n</i> (%)	737 (19.1)	124 (9.8)	613 (23.7)	< 0.001

prevalence of diabetes specifically in people with GOA and did not distinguish between type 1 or type 2 diabetes. Our study differs from the previous research because we included only patients with OA diagnosis who were further categorized as GOA or LOA. Another difference in the current study is the specification of diabetes diagnosis that has not been distinguished in previous studies [40]. Our study restricted risk factors (e.g., diabetes) for GOA to patients with diagnoses codes for T2DM and excluded type 1 diabetes. Therefore,

the current findings show that the prevalence of T2DM was approximately double in people with GOA compared with LOA in younger and older adults. However, our sample showed that the prevalence of T2DM in people with LOA was less than the reported prevalence in the general population [41]. The current study found the prevalence of diagnosed T2DM in LOA was 7.2% compared with 11.6 in the general population in the same age group (45–64 years). Further, the prevalence of diagnosed T2DM in LOA in our sample was

Table 3 The prevalence of diabetes in people with generalized and localized OA

Age groups	Type 2 diabetes	Generalized OA <i>N</i> = 1265	Localized OA <i>N</i> = 2590
45–64 years	Yes, <i>n</i> (%)	60 (17.8)	126 (7.2)
	Standardized residuals	4.0	– 2.0
	No, <i>n</i> (%)	277 (82.2)	1282 (91.1)
	Standardized residuals	– 1.4	0.7
65 years or older	Yes, <i>n</i> (%)	267 (28.8)	186 (15.7)
	Standardized residuals	4.8	– 4.3
	No, <i>n</i> (%)	661 (71.2)	996 (84.3)
	Standardized residuals	– 2.5	2.2
All age groups	Yes, <i>n</i> (%)	327 (25.8)	312 (12.0)
	Standardized residuals	8.1	– 5.7
	No, <i>n</i> (%)	938 (74.2)	2278 (88.0)
	Standardized residuals	– 3.6	2.5

Table 4 Logistic regression for the association of each risk factor with generalized OA

	Unadjusted OR (95% CI)	<i>p</i> value	Adjusted OR (95% CI)	<i>p</i> value
Age	1.07 (1.06–1.08)	<0.001	NA	
Sex	2.04 (1.77–2.36)	<0.001	NA	
Race	1.04 (0.93–1.15)	0.53	NA	
Type 2 DM	2.55 (2.14–3.03)	<0.001	2.21 (1.84–2.66)	<0.001
Hypertension	4.83 (4.17–5.59)	<0.001	3.68 (3.15–4.30)	<0.001
Dyslipidemia	6.49 (5.60–7.53)	<0.001	5.13 (4.39–5.99)	<0.001
Neuropathy	2.93 (2.15–3.99)	<0.001	2.58 (1.85–3.59)	<0.001
Body mass index	0.98 (0.96–1.00)	0.06	1.006 (0.98–1.03)	0.44

Adjusted OR: adjusted for age, gender, and race

15.7% compared with 21.3% in the general population [41]. These differences could be explained by our definition for diabetes as we included only T2DM with at least 2 ICD codes and other factors such as single site and using real-world clinical data versus survey data.

This study found that demographic factors including age, sex, and race were associated with OA. Aging has a negative impact on many systems and organs, and is associated with cellular function decline that has been linked to OA [42, 43]. Although aging is a known risk factor for OA, previous research has focused on LOA (e.g., knee, hip, or hand) [19, 21]. The current study adds to the literature in that increased age was more strongly associated with GOA compared with LOA. Our study showed that females increased the odds of GOA compared with males. A previous meta-analysis has indicated that females have a higher risk of OA after menopause [44], potentially due to age-associated hormonal changes. Race has also been shown to be associated with OA, with previous research reporting an association between non-Hispanic African Americans and OA using a national health survey in the USA [22]. However, our multivariable analysis did not identify this relationship. This could be attributed to the single

site for our data, resulting in a limited diversity of ethnicity in patients.

A common shared risk factor in OA and T2DM is obesity, which is associated with 90% of diabetes [45] and OA [46]. Obesity might be linked to OA due to the effect of weight and misalignment on joints [47]. However, previous research has also reported associations between obesity and OA of non-weight-bearing joints such as the hands [15], suggesting a potential systemic dysfunction. In contrast to these studies, our study did not find a statistically significant association between BMI and GOA. The current study utilized the multiple imputations method for the missing BMI; however, the results were comparable between both datasets. These findings are limited by the missing data from BMI in our sample, and the use of BMI data up to 1 year before or after the index date of OA diagnosis.

Type 2 diabetes as a metabolic syndrome has been associated with OA. Two meta-analyses were published investigating the association between OA and diabetes, and both showed a significant association between OA and diabetes [40, 48]. Although previous research found an association between diabetes and mainly LOA, our study observed an association with GOA versus LOA that has not been previously investigated. However, in contrast to our findings and previous reports, a third recent meta-analysis found little evidence for an association between diabetes and knee OA, and no evidence to support an association between diabetes and hip or hand OA [49]. This analysis included studies examining only LOA, specifically knee, hip, or hand OA, but GOA was not considered. Given this contradictory evidence, the relationships between diabetes and GOA, which may affect half of the people with OA, require further investigation.

Hypertension has also been found to be a risk factor for LOA [37]. Prior research demonstrated that the accumulation of metabolic factors including hypertension and diabetes was associated with the occurrence of knee OA over 3 years [15]. Hypertension is a systemic disease and contributes to multiple-joint OA through vascular impairments and decreased blood flow that lead to subchondral ischemia [50]. Our study found that people with hypertension are about 2

Table 5 Multiple logistic regression for the association of type 2 DM, hypertension, dyslipidemia, neuropathy, and body mass index with generalized OA

	Adjusted OR (95% CI)	<i>p</i> value
Age	1.05 (1.04–1.06)	<0.001
Sex	1.69 (1.41–2.02)	<0.001
Race	0.97 (0.84–1.11)	0.61
Type 2 DM	1.37 (1.05–1.78)	0.02
Hypertension	1.99 (1.63–2.43)	<0.001
Dyslipidemia	3.46 (2.86–4.19)	<0.001
Neuropathy	1.36 (0.91–2.05)	0.13
Body mass index	0.99 (0.97–1.01)	0.22

Adjusted OR: adjusted for age, gender, race, depression, anxiety, sleep disorders, medications (antidiabetics, antihypertensives, antilipemic, and antidepressants), and risk factors (diabetes, hypertension, dyslipidemia, neuropathy, and body mass index)

times more likely to have GOA compared with those without hypertension, even after controlling for other covariates including T2DM and hypertension medications.

Dyslipidemia indicates disturbances in serum levels of any form of cholesterol, including high-density lipoprotein, low-density lipoprotein, total cholesterol, or triglyceride. Previous studies have demonstrated the association between dyslipidemia, T2DM, and OA [15, 17]. Our study was consistent with this previous research, suggesting that patients with dyslipidemia are about 3 times more likely to have GOA compared with those without. In contrast, other investigations reported no association between T2DM, dyslipidemia, and OA [18]. This research focused on non-weight-bearing OA, included different definitions for dyslipidemia, and lacked control for medications and other confounders. This is important, because previous studies have shown that antilipemic medications such as statin are associated with a lower incidence and progression of knee OA [25].

This study has limitations to be considered. A retrospective design cannot lead to inferences of causality, and future research should examine the longitudinal impact of T2DM on GOA incidence. In addition, the study used data from a single site, and this may limit the generalizability of the results. Although two ICD-9 or ICD-10 diagnoses codes were used for each disease to improve accuracy, these codes are prone to potential measurement errors or bias. The sites for OA were not included in the analysis and future research should examine the association within the context of sites and symptoms. Future research should use objective measures of T2DM, such as A1c, and OA, such as X-ray and/or joint space narrowing. GOA diagnosis should be acknowledged as another limitation because of multiple different definitions and no universally accepted definition that can be used. Every effort has been made to capture possible confounding variables; however, there may be other factors associated with GOA that have not been included. Missing BMI values in the current study should also be acknowledged as a limitation. Although missing BMI values were imputed using a validated method [39], these imputations were based on data ranging from 1 year before or after the index date of OA diagnosis. Thus, BMI values used in the study may not reflect the actual BMI values at the time of data collection; BMI may have changed dramatically within a year. Therefore, the results should be interpreted with caution regarding BMI. The duration of OA, T2DM, or other risk factors was not included and could be an important area for future research. Despite these limitations, our study findings add to the current knowledge about diabetes and OA and add new information related to shared risk factors commonly found in each condition, diabetes and OA.

Conclusion

This study found a higher prevalence of T2DM in people with GOA when compared with LOA across all age groups using real-world clinical data, suggesting an increased susceptibility to GOA in T2DM. People with chronic diseases including T2DM, hypertension, and dyslipidemia had significantly and independently increased odds of GOA when compared with those without chronic diseases after controlling for other covariates. Future research should longitudinally examine the causality of this association between risk factors and GOA.

Author contributions All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted. Aqeel M Alenazi takes the full responsibility for this work.

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Data availability The dataset generated during the current study are not publicly available due to privacy agreement but are available from the corresponding author on reasonable request.

Compliance with ethical standards

Ethical approval All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration. This study received an exempt determination from the institutional review board for using de-identified data. An approval from the Data Request Oversight Committee was obtained for this analysis.

Disclosures None.

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