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# Association of hand or knee osteoarthritis with diabetes mellitus in a population of Hispanics from Puerto Rico

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## Abstract

**Background—**Although a higher prevalence of osteoarthritis (OA) has been reported among diabetes mellitus (DM) patients, inconsistencies and limitations of observational studies have precluded a conclusive association.

**Objective—**To evaluate the association of hand or knee OA with DM in a population of Hispanics from Puerto Rico.

**Methods—**A cross-sectional study was performed in 202 subjects (100 adult DM patients as per the National Diabetes Data Group Classification, and 102 non-diabetic subjects). OA of hand and knee was ascertained using the American College of Rheumatology classification criteria. Sociodemographic characteristics, health-related behaviors, comorbidities, pharmacotherapy and DM clinical manifestations were determined. Multivariable logistic regression was used to evaluate the association of DM with hand or knee OA, and to evaluate factors associated with hand or knee OA among DM patients.

**Results—**The mean (standard deviation, SD) age for DM patients was 51.6 (13.1) years; 64.0% were females. The mean (SD) DM duration was 11.0 (10.4) years. The prevalence of OA in patients with DM and non-diabetics subjects was 49.0% and 26.5%, respectively ($p<0.01$). In the multivariable analysis, patients with DM had 2.18 the odds of having OA when compared to non-diabetic subjects (95% CI: 1.12–4.24). In a sub-analysis among DM patients, female patients were more likely to have hand or knee OA (OR [95% CI]: 5.06 [1.66–15.66]), whereas patients who did not use insulin alone for DM therapy were more likely to have OA (OR [95% CI]: 4.44 [1.22–16.12]).

**Conclusion—**In this population of Hispanics from Puerto Rico, DM patients were more likely to have OA of hands or knees than non-diabetic subjects. This association was retained in multivariable models accounting for established risk factors for OA. Among DM patients, females were at greater risk for OA, whereas the use of insulin was negatively associated.

### Key indexing terms

diabetes mellitus; osteoarthritis; metabolic disorders; musculoskeletal disorders

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## INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by hyperglycemia, which results from the inability of the body to produce or use insulin [1]. High glucose levels may affect cell function and alter extracellular matrix components of the connective tissue producing damage [2–3]. In fact, a higher prevalence of connective tissue and musculoskeletal conditions occurs among DM patients [4]. Although changes in connective tissue physiology have been documented in DM; the pathophysiology leading to musculoskeletal disorders in patients with DM is not well understood.

Osteoarthritis (OA) is characterized by cartilage degeneration or degradation of one or more joints [5]. Hands and knees are the most common joints affected by OA. Previous studies have suggested that DM patients are at higher risk of developing rheumatic disorders [4, 6–8]; some have reported a correlation of OA with longer DM duration and poor glycemic control [6–9]. Furthermore, the presence of peripheral neuropathy in DM patients may increase the risk of aggressive forms of OA [10]. However, it is still unclear if diabetes mellitus is a risk factor for OA. Several discrepancies in previous works such as definitions for OA, and study limitations such as not including non-diabetic control groups or examining potential confounders have precluded the establishment of a definitive association. The present study aimed to evaluate the association of hand or knee OA among DM patients and to evaluate the factors associated with OA among these patients.

## METHODS

### Study Population

A cross-sectional study was performed in adult DM patients and non-diabetic subjects from Puerto Rico. DM patients were ≥ 21 years old and fulfilled the National Diabetes Data Group Classification which defines diabetes as present from any two of the following tests on different days: (1) symptoms of diabetes *plus* casual plasma glucose concentration ≥ 200mg/dL, or (2) fasting plasma glucose ≥ 126mg/dL, or (3) 2-hour plasma glucose ≥ 200mg/dL during an oral glucose tolerance test [11]. All participants were initially approached by the clinical investigators and asked to participate in a study about rheumatic conditions in diabetes mellitus. Possible candidates for the study were recruited from the outpatient endocrinology clinics at the University of Puerto Rico Medical Sciences Campus. For the recruitment of non-diabetic subjects the clinical investigators contacted control subjects; these included patients' friends or neighbors accompanying diabetic patients to their scheduled medical visit. This method of enrollment was more likely to provide a control population of similar socioeconomic-demographic features as the cases rather than sampling the general population given the fact that the cases were drawn as they presented to the endocrinology clinics for evaluation and/or treatment. Patients' relatives were excluded. The study period was from March 2006 to March 2008. An informed consent was obtained for all individuals willing to participate. The study was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus.

A complete medical examination was performed for each participant. A complete musculoskeletal examination in a standard fashion was performed by one of the two principal investigators. At study visit, a structured questionnaire was completed for each participant to gather data about sociodemographic features, health-related behaviors, clinical manifestations, and pharmacotherapy.

### Variables

OA of hand and knee was ascertained using the American College of Rheumatology (ACR) classification criteria [12–13]. ACR criteria for diagnosing hand OA required the presence

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of hand pain, aching, or stiffness *plus* hard tissue enlargement of at least 2 of 10 selected joints *plus* less than 3 swollen metacarpophalangeal joints *plus* either hard tissue enlargement of at least 2 distal interphalangeal joints *or* deformity of at least 1 of 10 selected joints [12]. ACR criteria for knee OA was based on clinical examination as knee pain in addition to 3 of the following 6 criteria: (1) more than 50 years of age, (2) less than 30 minutes of morning stiffness, (3) crepitus, (4) bony tenderness, (5) bony enlargement, or (6) an absence of palpable warmth [13].

Variables evaluated for all study participants included sociodemographic parameters, health-related behaviors, comorbidities, and pharmacotherapy. Sociodemographic features included gender, age, marital status, and level of education. Among health-related behaviors, smoking and exercise were evaluated. Comorbities included arterial hypertension, dyslipidemia (hypercholesterolemia and/or hypertriglyceridemia), obesity (defined as a body mass index [BMI] $\geq 30.0$ kg/m$^2$) rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), gout, chronic back pain, fibromyalgia, hypothyroidism, depression, and osteoporosis. Finally, the use of analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), and intra-articular injections was determined.

For DM patients, disease duration, fasting blood glucose, glycemic control, and DM long-term complications and pharmacotherapy were examined. Glycemic control was evaluated using an average of the previous three measurements of glycosylated hemoglobin (HgA1c). DM complications including renal disease (microalbuminuria, proteinuria, and end-stage renal disease [ESRD]), retinopathy (non-proliferative and proliferative), cataracts, neurologic complications (peripheral neuropathy, gastroparesis, neurogenic bladder, cerebrovascular accidents), and cardiovascular complications (coronary artery disease and peripheral arterial disease) were studied. Finally, the use of insulin and oral DM medications was ascertained.

## Statistical analysis

Univariable analysis was done using the mean (standard deviation, SD), median (25$^{th}$- and 75$^{th}$-percentiles) for continuous data, and frequencies and percentages for categorical data. Bivariable analysis was performed using the unpaired t-test (or Mann-Whitney U test for small sample size comparisons) for continuous data; chi-square statistics was employed to describe categorical data.

To study the association of DM status as well as sociodemographic characteristics, health-related behaviors, and clinical parameters with OA; contingency tables were constructed. Given that the present analysis was intended to compare DM status and known risk factors for OA in subjects with and without hand or knee OA, we calculated age- and sex-adjusted odd ratios (ORs) and their 95% confidence intervals (CIs) for all the parameters of interest. Due to the fact that DM and OA are both associated with age and BMI, we also calculated age- and BMI-adjusted OR (95% CI). Finally, an unconditional multivariable logistic regression analysis was done to evaluate the association between DM and OA after adjustment for the following selected OA risk factors: gender, age, education level, BMI, exercise, and osteoporosis. Statistical significance was set at $p<0.05$.

A sub-analysis was done among diabetic subjects to evaluate the association of sociodemographic characteristics, health-related behaviors, clinical parameters and pharmacological therapy with OA. Contingency tables and ORs (95% CIs) were also calculated to examine the association of the study variables with hand or knee OA. Finally, a multivariable unconditional logistic regression analysis was performed to evaluate the factors associated with hand or knee OA among diabetic subjects; variables with a $p<0.05$ in

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bivariable analysis were included in the multivariable analysis. Statistical significance was set at $p<0.05$.

The statistical software STATA *version 11* (STATA Corp, College Station, TX, USA) was used to performed the analysis.

## RESULTS

A total of 217 subjects were asked to participate in the study, 15 patients declined to participate. The complete sample consisted of 202 subjects, 100 DM patients and 102 non-diabetic individuals. The mean (SD) age for DM patients was 53.3 (12.9) years, whereas the mean (SD) of non-diabetic subjects was 50.0 (13.1). The proportion of females and males DM patients and non-diabetic subjects was 64.0% vs. 64.7% and 36.0% vs. 35.3%, respectively. DM patients were more likely to have <12 years of formal education than non-diabetic subjects (45.5% vs. 30.4%, p-value=0.02). In addition, DM patients were more likely ($p<0.01$) to have hypertension (68.0% vs. 25.5 %), dyslipidemia (62.0% vs. 18.6%), and obesity (57.0% vs. 31.4%). No significant differences were observed for exercise and smoking. The overall prevalence of hand or knee OA was 37.6%. The prevalence of OA among diabetic patients was 49.0%, whereas the prevalence of OA among non-diabetic subjects was 26.5% ($p<0.01$). Among diabetic patients, two had SLE, five had fibromyalgia syndrome, and none had rheumatoid arthritis or gouty arthritis. Among non-diabetic subjects, one had gouty arthritis, one had fibromyalgia syndrome, and none had RA or SLE.

To evaluate the factors associated with OA in the complete study sample (n=202), we performed an analysis comparing subjects with hand or knee OA (37.6%) and subjects without OA (62.4%) (Table 1). Patients with hand or knee OA were more likely to have <12 years of formal education, and to be female, older, and less physically active than subjects without OA ($p<0.05$). Also, subjects with hand or knee OA were more likely to have DM, obesity (BMI ≥ 30.0 kg/m$^2$), hypertension, major depression, and osteoporosis than non-OA subjects ($p<0.05$). A marginal tendency was observed for dyslipidemia among patients with OA ($p=0.05$). No association was observed between OA and rheumatic diseases such as RA, SLE, gout and fibromyalgia (data not shown). In addition, the use of analgesics and NSAIDs were significantly higher among patients with hand or knee OA than among non-OA subjects (30.3% vs. 9.5% and 19.7% vs. 5.6%, respectively; $p<0.05$). Only 3 (3.9%) of OA patients reported having being treated with intra-articular injections.

### Association of hand or knee OA with DM

Table 2 shows the ORs and 95% CIs for the association of hand or knee OA with diabetes. In age- and sex-adjusted analysis, DM patients had a 2.72 fold increased risk of hand or knee OA (95 CI%: 1.49–4.96). In a model controlling for the effects of age and obesity, the odds of OA in DM patients decrease to 2.36 (95% CI: 1.26–4.42). In the multivariable analysis, after adjustment for established risk factors for OA (age, sex, education level, obesity, exercise, and osteoporosis) DM patients had 2.18 fold increased risk of hand or knee OA compared to non-diabetic subjects (95%CI: 1.12–4.24).

### Factors associated with hand or knee OA among diabetic patients

Factors associated with hand or knee OA among the 100 diabetic patients are depicted in table 3. From the sociodemographic domain, female gender, older age, and education level (<12 years) were associated with the presence of hand or knee OA ($p<0.05$). Diabetic patients with OA were more likely to be obese and to suffer from depression, and less likely to smoke and to be physically active than diabetics without OA ($p<0.05$). No significant differences were observed for disease duration, DM type (1 or 2), hypertension,

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dyslipidemia, osteoporosis, HbA1c levels, and FBG levels. DM patients with OA were more likely to suffer renal (48.9% vs. 29.4%; p=0.045), cardiovascular complications (42.9% vs. 23.5%; p=0.04), and chronic back pain (57.1% vs. 25.5%; p=0.01) than non-OA diabetic patients (57.1% vs. 25.5%; p=0.01). Evaluation of comorbid rheumatic conditions (RA, SLE, gout, and fibromyalgia) and hypothyroidism showed no significant differences between diabetics with OA and non-OA diabetic subjects (data not shown). No statistical difference was observed for the use of oral medications alone or a combination of insulin and oral medications between OA and non-OA diabetic patients (32.7% vs. 27.5% and 51.0% vs. 37.3%, respectively). However, patients with OA were less likely to use insulin alone than patients without OA (14.3% vs. 35.3%; $p<0.05$).

Table 4 shows the factors associated with hand or knee OA among DM patients. In the bivariable analysis, the odds for hand or knee OA were significantly increased among DM patients who were older, female, had < 12 years of formal education, obese, less physically active, depressed, had renal and cardiovascular complications. In addition, no use of insulin was significantly associated with hand or knee OA. Female gender and no use of insulin remained statistically associated with hand or knee OA in the multivariable analysis after adjustment for age, education level, obesity, exercise, depression, and renal and cardiovascular complications. DM female patients had a 5 fold increased risk of hand or knee OA compared to DM male patients (95% CI: 1.66–15.56). DM patients who did not use insulin alone for DM treatment had a 4.44 fold increased risk of hand or knee OA (95% CI: 1.22–16.12).

## DISCUSSION

The present study evaluated the association of OA with diabetes among Hispanics from Puerto Rico, a group with a significant burden of DM [14]. We found that patients with DM were more likely to have hand or knee OA than non-diabetic subjects. This association was retained in models adjusting for sex and age, age and BMI, as well as in multivariable models accounting for established risk factors for OA. In the multivariable analysis among DM patients, female gender was associated with an increased risk for hand or knee OA, whereas the use of insulin was negatively associated with OA.

Population-based studies performed in the US using data of the third National Health and Nutrition Examination Survey (NHANES III), have documented a higher prevalence of OA among subjects with DM. Singh and colleagues estimated the prevalence of DM among OA subjects in 11% compared to a prevalence of 6% in the general population without OA [15]. This study had some limitations including the ascertainment of OA which was based on self-report and not on clinical grounds. In a recent study using the same NHANES III data, Puenpatom et al found that hyperglycemia was significantly prevalent among subjects with OA (using ICD-9 code, radiographic evidence of OA, or history of being told by a physician that they had OA) compared to the population without OA (30.7% vs. 11.2%, respectively) [16]. Even though a higher prevalence of OA among DM subjects has been documented, epidemiological evidence of the association between DM and OA still remains unclear. Some studies have reported an association between DM with radiological knee OA [17], foot and knee OA [18], and between poor glycemic control and risk of OA [19]; while some studies have shown no association between non-insulin dependent DM and OA [20, 21]. Due to inconsistencies and limitations in observational studies, a conclusive association between DM and OA has not been reached. A possible explanation for the latter is that the role of potential confounders such as age, gender, obesity, exercise, and metabolic factors were not thoroughly examined in these studies [22].

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Type 2 DM is a metabolic disorder characterized by high glucose levels as a result of insulin resistance and relative insulin deficiency [23]. Disorders that affect glucose metabolism may favor the development or progression of OA. For example, in a study evaluating the ability of chondrocytes to regulate their glucose transport capacity in extreme conditions of extracellular glucose (either insufficient or excessive), it was found that normal chondrocytes were capable to adjust to variations of extracellular glucose concentrations (modulating the glucose transporter 1 [GLUT-1] synthesis) whereas chondrocytes from OA patients were unable to downregulate GLUT-1 resulting in accumulation of glucose and higher production of reactive oxygen species. This may constitute a pathogenic mechanism by which conditions such as DM could promote degenerative changes that facilitate the progression of OA [24]. Rojas-Rodríguez et al reported that pathogenesis of obesity-induced OA may be explained by the metabolic changes in the striated muscle induced by the interaction of insulin resistance and systemic inflammation in obese individuals [25]. It is also known that pro-inflammatory molecules are among critical mediators of the disturbed processes implicated in OA pathophysiology [26]. Likewise, increased levels of markers and mediators of inflammation and acute-phase reactants such as fibrinogen, C-reactive protein, interleukin-6, plasminogen activator inhibitor (PAI-1) are elevated in patients with type 2 DM [27].

Age is a well-established factor associated both with DM and OA [28, 29], suggesting the possibility of an association by chance of these conditions [30]. Despite this fact, an increased prevalence of OA among younger DM patients, rather than older individuals, has been reported [15]. Another study supported this observation when an effect modification was noted with a significant burden of OA among younger DM patients; the interaction remained significant even after adjusting for DM duration and BMI [31]. In our study, we performed an additional analysis stratifying by age and we observed a three-fold increase risk of OA among subjects <60 years of age with diabetes (95% CI 1.39–6.11), but not for patients with diabetes ≥60 years (OR [95% CI]: 2.06 [0.69–6.16]). The results for individuals <60 years of age remained significant after controlling for BMI (OR [95% CI]: 2.63 [1.23–5.64]). The latter suggests that the association between OA and DM might not necessarily be explained by aging but by other systemic factors. The fact that OA complications are observed at younger age in DM patients when compared to their counterparts in the general population highlights the need to examine this association further [8].

An increased prevalence of metabolic syndrome and OA particularly among younger individuals has been previously acknowledged [16, 29, 31]. Thus, we evaluated the correlation of OA with metabolic factors such as obesity, arterial hypertension and dyslipidemia. In the age- and sex-adjusted analysis, we found an association for obesity and arterial hypertension but not in the multivariable analysis adjusted by age, sex, education, DM, osteoporosis, and obesity. No association was found for dyslipidemia. In a previous study evaluating the association of hand OA with metabolic components, a strong correlation was observed between diabetes and obesity but not with hypertension and dyslipidemia [31]. These results suggest that diabetes and obesity might play an important role in the pathogenesis of OA whereas hypertension and dyslipidemia might occur as consequence of diabetes and obesity.

It is also important to acknowledge the role of exercise in the management of OA. It is known that one of the most prevalent risk factors for function decline in daily activities among patients with hip or knee OA is the lack of physical activity [32, 33]. Moreover, regular exercise is associated with a lower prevalence of obesity, and diabetes, among other cardiovascular factors highly related to OA [34]. It has also been suggested that exercise programs are beneficial for reducing pain and improving physical performance [35]. In our

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study we found a decrease in the risk of OA among physically active subjects both in age- and sex-adjusted model but not in the multivariable model. However, we could not determine if the lack of physical activity in patients with OA was a risk factor or a result of the pain or disability caused by the disease. A recent meta-analysis found an association between low level of physical activity with a low level of physical function among subjects with hip and knee OA, although the correlation was modest [36]. Since all studies evaluated in the meta-analysis were cross-sectional, longitudinal studies are needed to further evaluate the role of exercise among OA patients.

In agreement with other studies [37, 38] we found that women were more likely to have OA. However, a previous study did not find gender differences in the risk of self-reported OA and non-insulin dependent diabetes mellitus [21]. Thus, additional studies are needed to further evaluate the increased risk of hand or knee OA among women.

We found a lower proportion of hand or knee OA among diabetic patients who were using insulin. Chondrocytes have limited regenerative and reparative capacities [39]. Growth factors have a role in the preservation of the cartilage matrix [40]. Indeed, concentrations of insulin growth factor 1 correlates with OA, with lower concentrations of IGF 1 observed among OA patients compared to control subjects [41]. Therefore, IGF 1 could play an important role in the development of OA [40, 41], and may also contribute to cartilage degradation [42, 43]. Interestingly, in a study examining the role of insulin as a potential treatment for arthritis, it was shown that insulin had positive effects on the matrix metabolism of isolated chondrocytes and articular cartilage [44]. Based on the results of these works and the negative association with OA that we found in our cross-sectional study, longitudinal studies are required to examine if insulin is a potential protector against OA.

Our study has some limitations. First, this work has the limitations inherent to a cross-sectional study. Second, this study was performed in a Hispanic group evaluated in a tertiary medical center in San Juan, Puerto Rico; thus, the results are not intended to be generalized to the entire population of Puerto Rico or to apply to other ethnic group. Third, DM status of non-diabetic subjects was self-reported; therefore, the possibility of misclassification bias must be acknowledged; however, the effect of the misclassification would be to underestimate the association of DM and OA, not to overestimate the association. Fourth, the statistical significance of covariates such as smoking and osteoporosis could be affected by a low reported frequency. Fifth, not all patients had X-rays available. Nonetheless, the diagnostic criteria that we used for hand and knee OA do not require imaging studies for classification. Finally, other risk factors for OA such as hormonal replacement therapy, occupational and sports activities, and genetic factors were not evaluated.

Despite these limitations, the present study has important clinical implications. Contrary to other publications, the definition of OA did not rely on self-report but on clinical evidence of OA performed by specialized and qualified personnel. Forty-nine percent of DM subjects had hand or knee OA; this proportion is higher than that reported in other series. Moreover, we were able to find a statistical association between DM and hand or knee OA, even after adjustment for other known risk factors for OA. This is a significant finding especially considering the high prevalence of diabetes among Hispanics from Puerto Rico. Strategies to reduce the burden of additional metabolic factors associated with OA must be addressed among this high-risk group to reduce physical limitations associated with OA and to improve quality of life. Even though we did not find a significant difference of glycemic control between DM patients with and without OA, a tendency towards a poorer glycemic control among those with OA was observed. Careful attention must be addressed to the need of metabolic control to improve outcomes among DM patients. Identification of DM

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individuals at high risk for OA is essential for the improvement and maintenance of a good quality of life.

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## KEY POINTS

1. Puerto Rican patients with diabetes mellitus had 2.18 the odds of having OA when compared to non-diabetic individuals.
2. This association was retained in multivariable models accounting for established risk factors for OA.
3. Among diabetic patients, females were more likely to have hand or knee OA, whereas patients who used insulin therapy were less likely to have OA.

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## Table 1

Sociodemographic, health-related behaviors, selected comorbities, and pharmacotherapy in the complete study sample* (N=202).

| Features | Complete sample (N=202) | | |
|---|---|---|---|
| | OA (n=76) | Non-OA (n=126) | p-value |
| **Gender,** female | 56 (73.7) | 74 (58.7) | 0.03 |
| **Age,** mean (SD) *years* | 57.6 (13.1) | 48.1 (13.8) | <0.01 |
| **Marital status,** married | 49 (64.5) | 78 (61.9) | 0.71 |
| **Education,** < 12 years | 43 (56.6) | 34 (27.2) | <0.01 |
| **Smoking** | 7 (9.2) | 14 (11.1) | 0.67 |
| **Exercise** | 13 (17.1) | 46 (36.5) | <0.01 |
| **Obesity** (BMI ≥ 30.0, $kg/m^2$) | 43 (56.6) | 46 (36.5) | 0.01 |
| **Diabetes** | 49 (64.5) | 51 (40.5) | <0.01 |
| **Hypertension** | 48 (63.2) | 46 (36.5) | <0.01 |
| **Dyslipidemia** | 37 (48.7) | 44 (34.9) | 0.05 |
| **Depression** | 25 (32.9) | 16 (12.7) | <0.01 |
| **Osteoporosis** | 7 (9.2) | 3 (2.3) | 0.03 |
| **Analgesics** | 23 (30.3) | 12 (9.5) | <0.01 |
| **NSAIDs** | 15 (19.7) | 7 (5.6) | <0.01 |
| **Intra-articular injections** | 3 (3.9) | 0 (0) | - |

* Data are frequencies (percentages) unless otherwise stated; OA: osteoarthritis; NSAIDs: non-steroidal anti-inflammatory drugs; SD: standard deviation

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## Table 2

Association of diabetes with hand or knee osteoarthritis in the complete study sample (N=202).

| **Factors** | ***Hand or Knee OA; OR (95% CI)*** | | |
|---|---|---|---|
| | **Age- and sex- adjusted model** | **Age- and BMI- adjusted model** | **Multivariate model†** |
| Diabetes mellitus | 2.72 (1.49–4.96) | 2.36 (1.26–4.42) | 2.18 (1.12–4.24) |

OR (95% CI): odd ratios (95% confidence interval);

†Multivariate model *(n=200)*: adjusted by age (≥ 60 years), gender (female), education (<12 years), BMI (≥ 30 kg/$m^2$), exercise, and osteoporosis.

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## Table 3

General characteristics, glycemic control and glucose level, DM complications and treatment modalities among diabetes subjects by osteoarthritis status (n=100)*

| General characteristics | OA status | | |
|---|---|---|---|
| | OA (n=49) | Non-OA (n=51) | p-value |
| **Gender,** female | 38 (77.6) | 26 (51.0) | 0.01 |
| **Age,** mean (SD) years | 57.5 (10.4) | 49.4 (13.9) | <0.01 |
| Median (25th- and 75th percentiles) | 59.5 (52.8, 63.0) | 52.3 (40.5, 59.2) | |
| **Diabetes type** | | | |
| **1** | 4 (8.2) | 10 (19.6) | 0.10 |
| **2** | 45 (91.8) | 41 (80.4) | |
| **Disease duration,** mean (SD) years | 11.2 (10.6) | 10.9 (10.4) | 0.90 |
| **Marital status,** married | 29 (59.2) | 36 (70.6) | 0.23 |
| **Education,** <12 years | 31 (63.3) | 5 (30.0) | <0.01 |
| **Smoking** | 3 (6.1) | 10 (19.6) | 0.05 |
| **Exercise** | 9 (18.4) | 21 (41.2) | 0.01 |
| **Obesity** (BMI ≥ 30.0, kg/m$^2$) | 33(67.4) | 24 (47.1) | 0.04 |
| **Hypertension** | 37 (75.5) | 31 (60.8) | 0.12 |
| **Dyslipidemia** | 33 (67.4) | 29 (56.9) | 0.28 |
| **Osteoporosis** | 5 (10.2) | 3 (5.9) | 0.48 |
| **Osteomyelitis** | 2 (4.1) | 3 (5.9) | >0.99 |
| **Depression** | 18 (36.7) | 7 (13.7) | <0.01 |
| **Glycemic control and glucose level** | | | |
| **HbA1c,** mean (SD) | (n=48) 8.3 (2.3) | (n=47) 7.9 (2.3) | 0.42 |
| **Fasting blood glucose,** Mean (SD) | (n=47) 163.2 (85.9) | (n=27) 146.6 (87.4) | 0.36 |
| **DM Complications** | | | |
| **Renal** | 24 (48.9) | 15 (29.4) | 0.05 |
| Microalbuminuria | 10 (20.4) | 9 (17.7) | 0.73 |
| Proteinuria | 13 (26.5) | 6 (11.8) | 0.06 |
| ESRD | 1 (2.0) | 2 (3.9) | >0.99 |
| **Retinopathy** | 11 (22.5) | 12 (23.5) | 0.90 |
| Proliferative | 5 (10.2) | 8 (15.7) | 0.42 |
| **Cataracts** | 11 (22.5) | 7 (13.7) | 0.26 |
| **Neurologic** | 26 (53.1) | 25 (49.0) | 0.69 |
| Peripheral neuropathy | 23 (46.9) | 21 (41.2) | 0.56 |
| Gastroparesis | 0 (0) | 2 (3.9) | 0.50 |
| Neurogenic bladder | 7 (14.3) | 1 (2.0) | 0.03 |
| Cerebrovascular accident | 5 (10.2) | 2 (3.9) | 0.26 |
| **Cardiovascular** | 21 (42.9) | 12 (23.5) | 0.04 |
| Coronary Artery Disease | 15 (30.6) | 9 (12.2) | 0.13 |
| Peripheral arterial disease | 12 (24.5) | 5 (9.8) | 0.05 |

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| General characteristics | OA status | | |
|---|---|---|---|
| | OA (n=49) | Non-OA (n=51) | p-value |
| **Treatment modalities** | | | |
| **Insulin alone** | 7 (14.3) | 18 (35.3) | 0.02 |
| **Oral medications alone** | 16 (32.7) | 14 (27.5) | 0.57 |
| **Oral medications + insulin** | 25 (51.0) | 19 (37.3) | 0.17 |

* Data are frequencies (percentages) unless otherwise stated; OA: osteoarthritis; SD: standard deviation; HbA1c: glycosylated hemoglobin; ESRD: end-stage renal disease; CAD: coronary artery disease (includes: myocardial infarction, angina, percutaneous transluminal coronary angioplasty, and coronary artery bypass graft surgery).

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**Table 4**

Factors associated with osteoarthritis in diabetic subjects (N=100).

| **Factors** | ***Hand or Knee OA; OR (95% CI)*** | |
|---|---|---|
| | **Unadjusted model** | **Multivariate model (n=99)** |
| **Age** | 1.06 (1.02–1.10) | 1.04 (0.99–1.09) |
| **Gender,** female | 3.32 (1.40–7.90) | 5.06 (1.66–15.56) |
| **Education level,** <12 years | 4.02 (1.74–9.29) | 2.79 (0.95–8.24) |
| **BMI,** ≥ 30 kg/m$^2$ | 2.32 (1.03–5.22) | 1.37 (0.46–4.07) |
| **Smoking** | 0.27 (0.07–1.04) | - |
| **Exercise** | 0.32 (0.13–0.80) | 0.67 (0.20–2.26) |
| **Depression** | 3.65 (1.36–9.79) | 3.04 (0.80–11.58) |
| **Renal complications** | 2.30 (1.01–5.24) | 1.88 (0.64–5.56) |
| **Neurogenic bladder** | 8.33 (0.99–70.48) | - |
| **Cardiovascular complications** | 2.44 (1.03–5.76) | 1.91 (0.60–6.10) |
| **No use of insulin alone** | 3.27 (1.22–8.76) | 4.44 (1.22–16.12) |

OR (95% CI): odd ratios (95% confidence interval); age: analyzed as a continuous variable; BMI: Body mass index; Variables smoking and neurogenic bladder were excluded from multivariable analysis