Arthritis and Risk of Cognitive and Functional Impairment in Older Mexican Adults

Sreenivas P. Veeranki, MBBS, DrPH¹, Brian Downer, PhD¹, Daniel Jupiter, PhD¹, and Rebeca Wong, PhD¹

Abstract
Objective: This study investigated the risk of cognitive and functional impairment in older Mexicans diagnosed with arthritis. Participants included 2,681 Mexicans, aged ≥60 years, enrolled in the Mexican Health and Aging Study cohort. Method: Participants were categorized into arthritis and no arthritis exposure groups. Primary outcome included participants categorized into “cognitively impaired” or “cognitively normal” groups. Secondary outcomes included participants categorized into Normal, Functionally Impaired only, Cognitively Impaired only, or Dementia (both cognitively and functionally impaired) groups. Multivariable logistic and multinomial regression models were used to assess the relationships. Results: Overall, 16% or 7% were diagnosed with cognitive impairment or dementia. Compared with older Mexicans without arthritis, those who were diagnosed with arthritis had significantly increased risk of functional impairment (adjusted odds ratio [OR] 1.82, 95% confidence interval [CI] = [1.45, 2.29]), but not of dementia. Conclusion: Arthritis is associated with increased risk of functional impairment, but not with dementia after 11 years in older Mexicans.

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Introduction

Dementia, characterized by cognitive and physical decline, has emerged as a significant public health challenge in recent years (Prince et al., 2013; Wimo et al., 2013). According to the 2014 World Alzheimer’s Report (2014), approximately 44 million people currently live with dementia, which is expected to double by 2030 and triple by 2050. A recent meta-analysis estimated that Latin America has the highest age-adjusted prevalence of dementia at 8.5%, and this prevalence is expected to quadruple by 2050 (Prince et al., 2013). Despite the high prevalence of dementia in Latin America, the epidemiologic information regarding dementia in Mexico and other Latin American countries remains scarce (Llibre Rodriguez et al., 2008; Sosa et al., 2012). Approximately 58% of people with dementia currently live in low- and middle-income countries (LMICs), such as Mexico, and older adults in these countries are vulnerable to the rising dementia rates projected over the next few decades (Prince et al., 2013). Therefore, it is important to identify risk factors that may contribute to an increase in the prevalence of cognitive impairment or dementia among older adults in LMICs such as Mexico.

Several developmental and early-life risk factors (fetal length, head circumference, education), psychological factors (depression, anxiety disorders, psychological distress, and sleep disorders), lifestyle factors (smoking, alcohol, physical activity, cognitive stimulation, and diet), and comorbid factors (hypertension, diabetes, obesity, and dyslipidemia) contribute to the etiology of cognitive and functional impairment (Dillon et al., 2013; Ferri, Ames, Prince, & Dementia Research Group, 2004; Harrison et al., 2014; Kamogawa et al., 2010; Larson, Kukull, Buchner, & Reifler, 1987; Nash & Fillit, 2006; Okusaga et al., 2013; Panza et al., 2012; Petersen et al., 1997; Singh-Manoux & Schmidt, 2015; Thomas & Rockwood, 2001; Xia et al., 2015). Another comorbid disease of interest is arthritis, which may be associated with risk of cognitive and functional impairment, potentially through a systemic inflammatory response or comorbid cardiovascular risk factors (Maradit-Kremers et al., 2005; Roifman, Beck, Anderson, Eisenberg, & Genest, 2011; Shin, Katz, Wallhagen, & Julian, 2012).

Arthritis is a chronic disease of joints characterized by pain, swelling, and stiffness of joints. The most common types are osteoarthritis and rheumatoid arthritis. Osteoarthritis is a non-inflammatory aging wear-and-tear disease that is characterized by the loss of articular cartilage, bone hypertrophy, and
thickening of the joint capsule. Rheumatoid arthritis is a systemic autoimmuno-inflammatory disease characterized by a symmetrical persistent synovitis of the small joints, joint tenderness, pain, motion limitation, and morning stiffness, along with fatigue, generalized weakness, loss of weight, and low-grade fever (Creemers & Van de Putte, 2004). The global prevalence of arthritis is increasing, with the highest rates in Latin America and Caribbean countries (Prince, 2001). Epidemiological studies including case-control, prospective cohort, and hospital- and registry-based studies have investigated whether arthritis is a risk factor for cognitive and functional impairment, with inconsistent results (Breitner et al., 1994; de Jongh et al., 2011; French et al., 1985; Heyman et al., 1984; Jenkinson, Bliss, Brain, & Scott, 1989; McGeer, McGeer, Rogers, & Sibley, 1990). Given the sparse epidemiologic studies on arthritis or dementia in Mexico along with high prevalence estimates of these conditions, we investigated the association of arthritis with risk of cognitive and functional impairment after 11 years of follow-up among 2,681 Mexican adults aged ≥60 years enrolled in the Mexican Health and Aging Study (MHAS) cohort. Because several social, demographic, and comorbid conditions influence the association between arthritis and cognitive impairment, we adjusted for potentially important sociodemographic characteristics, lifestyle factors, and health conditions (Baumgart et al., 2015; M. H. Chen et al., 2014; Etgen, Sander, Bickel, & Forstl, 2011; Hughes & Ganguli, 2010; Rizzi, Rosset, & Roriz-Cruz, 2014; Srisuwan, 2013; van der Flier & Scheltens, 2005).

Method

Study Cohort and Population

Data from the MHAS were used to conduct this study. MHAS cohort profile and description of data elements have been presented previously (Wong, Michaels-Obregon, & Palloni, 2015). Briefly, the MHAS is the first longitudinal prospective cohort study of aging individuals in Mexico designed to understand the aging process and its disease, and disability burden among adults aged 50 years and older, and born prior to 1951. The cohort was established with initial recruitment of 15,186 participants in 2001 (Wave I). Follow-up observations were completed in 2003 (Wave II) and 2012 (Wave III). Wave II included 14,250 participants from Wave I, and Wave III included 18,465 participants (inclusive of 6,644 born during 1952-1961 new individuals and spouses). The response rates were 91.8% (Wave I), 93.3% (Wave II), and 88.1% (Wave III). Information on socioeconomic characteristics, migration, health conditions, disability, and family networks was obtained in all
three waves. Participants in Waves I (2001) and II (2003) are very similar, and differences in functional or cognitive impairment cannot be detected within 2 years; therefore, data from Waves I and III were used to conduct this study.

A summary of the selection of the final sample is presented in Figure 1. A total of 7,171 participants were aged ≥60 during Wave I, and 3,787 of these participants were interviewed during Wave III. The final sample included 2,681 participants who received a direct interview during Wave I, completed ≥2 cognitive assessments and had functional assessments with no evidence of cognitive and functional impairment during Wave I, had available data for covariates during Wave I (see study measures below), and completed ≥2 cognitive assessments or had a proxy measure of cognitive assessment during Wave III. Compared with participants included in the final sample (n = 2,681), participants with missing data for cognition, functional status, or covariates were significantly older, more likely to have never completed any years of formal education, to be male, to have experienced a stroke, to have never smoked, and to have never consumed alcohol. The Institutional Review
Board of the corresponding author’s institution approved the use of the MHAS cohort.

**Study Measures**

The study outcome was participants’ cognitive and/or functional impairment after 11 years (Wave III). Cognitive functioning for participants who received a direct interview was assessed using the brief version of the Cross-Cultural Cognitive Examination (CCCE), which is a validated screening instrument for epidemiological and cross-cultural assessment of individuals for cognitive functioning status (Glosser et al., 1993). A detailed description of the CCCE and its implementation in the MHAS cohort has been provided by Mejia-Arango, Wong, and Michaels-Obregón (2015). The CCCE instrument included attributes particularly tailored to older Mexican adults, and has been previously validated in Guam and U.S. mainland samples with 94% specificity and 99% sensitivity for dementia (Mejia-Arango & Gutierrez, 2011). Using this instrument, participants’ cognitive functioning status in both waves (Waves I and III) was assessed across five cognitive domains using five items each: verbal learning (8-word list immediate recall), verbal memory (8-word list delayed recall), visual–constructive abilities (drawing two figures in 90 s), visual memory (delayed recall of the figures previously drawn), and attention (visual scanning). Additional measures for orientation (date naming), verbal fluency (animal naming), and numeracy (counting backward) were supplemented to the instrument and administered to cohort participants in Wave III. Using the diagnostic criteria set by the National Institute on Aging–Alzheimer’s Association workgroups (McKhann et al., 2011), we ascertained an elderly adult as cognitively impaired if he or she performed $\geq 1.5 SD$ lower than what would be expected based on his or her age and years of education completed, and categorized participants into cognitively normal or impaired. This definition and cutoff point has been previously validated in a sample of 173 patients from the memory clinic of the Instituto Nacional de Ciencias Medicas y Nutricion in Mexico City, where the cognitively impaired status defined using the questionnaire was compared with dementia diagnosis using the *Diagnostic and Statistical Manual of Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 1994; Mejia-Arango & Gutierrez, 2011). Those participants who reported being impaired on at least three out of five cognitive domains were categorized into “cognitively impaired” group.

In addition to the CCCE instrument, a brief version of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE; Jorm, 1994) was used to assess cognitive functioning status of the participants from the
informants (family members or close relatives) of the participants who were unable to receive a direct interview during Wave I due to limitations in health, language issues, or other reasons. The IQCODE includes 16 questions and was administered to the informant who had knowledge about participant’s daily functioning. The informant rated the participant’s cognitive status during the time of instrument administration, comparing it with how it was 2 years earlier. Informants’ responses to each question were scored on the 5-point Likert-type scale and totaled to obtain the overall score, and an average score was calculated. Using the IQCODE, we ascertained participants as cognitively impaired if they scored an average of ≥3.4 on the IQCODE, and categorized them into cognitively normal or impaired. This instrument has been previously validated against clinical diagnosis among patients, and a cutoff point of 3.4 for defining cognitive impairment status was used. This was based on an earlier study conducted using community samples, where the cutoff point of 3.4 average score yielded 89% sensitivity and 94% specificity (Jorm, 2004).

Functional status of cohort participants was assessed by obtaining information about their basic Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs). ADLs included walking, bathing and eating, going to bed, and going to the bathroom, and IADLs included preparing a hot meal, shopping for groceries, taking medications, and managing money. Similar to earlier studies (Mejia-Arango & Gutierrez, 2011), study participants who needed assistance in ≥1 ADL or ≥2 IADLs were ascertained as being functionally impaired. Using this definition, study participants were categorized into two groups, namely, “functionally normal” or “functionally impaired.”

Using cognitive assessments, we defined our primary study outcome into two groups, namely, (a) cognitively normal and (b) cognitively impaired during Wave III. Similarly, using the two groups for cognitive functioning status, and the two groups for physical functioning status, we defined secondary study outcome by categorizing study participants into four groups: (a) Normal group—included participants who were neither cognitively nor functionally impaired, (b) Functionally Impaired only group—included participants who were functionally but not cognitively impaired, (c) Cognitively Impaired only group—included participants who were cognitively but not functionally impaired, and (d) Dementia group—included participants who were both cognitively and functionally impaired. This categorization allowed us to understand the relationship of arthritis and dementia as well as the relationship between arthritis and mild cognitive impairment, which is similar to Cognitively Impaired only group in our study. Participants in the Cognitively Impaired only group can exhibit three profiles of disease progression, which
include improvement, stability, or declining to dementia (Larrieu et al., 2002; Tuokko et al., 2003).

The study exposure was participants’ physician diagnosis of arthritis at Wave I. Study exposure was obtained using participants’ self-reported response to the question, “Has a doctor or medical personnel ever told you that you have arthritis or rheumatism?” Using participants’ self-report responses, we categorized them as being diagnosed with arthritis or not.

Based on the existing literature and plausible associations with both cognitive and functional impairment, and arthritis in older adults, participant sociodemographic characteristics, lifestyle factors (smoking and alcohol consumption), and health conditions (diabetes, hypertension, heart attack, stroke, depression) at baseline were included as covariates in the multivariable logistic regression models (Baumgart et al., 2015; M. H. Chen et al., 2014; Etgen et al., 2011; Hughes & Ganguli, 2010; Rizzi et al., 2014; Srisuwan, 2013; van der Flier & Scheltens, 2005)(Dillon et al., 2013; Ferri et al., 2004; Harrison et al., 2014; Kamogawa et al., 2010; Larson et al., 1987; Nash & Fillit, 2006; Okusaga et al., 2013; Panza et al., 2012; Petersen et al., 1997; Singh-Manoux & Schmidt, 2015; Thomas & Rockwood, 2001; Xia et al., 2015). Participant sociodemographic characteristics included age, highest level of educational attainment (0, 1-6, and ≥7 years), gender (male/female), and marital status (no/yes). Information on participants’ health conditions was obtained using self-reported responses about having ever been diagnosed by a physician with diabetes (no/yes), hypertension (no/yes), heart attack (no/yes), and stroke (no/yes). Depressive symptoms were measured using the adapted nine-item version of the Radloff’s Center for Epidemiological Studies–Depression Scale (CES-D). A binary no/yes response for each question was included rather than the original four-item response. We defined an older adult being depressed if he or she reported depressive symptoms on six or more items out of the nine items of the CES-D (Abuan, Yeager, & Montgomery, 2010; Ayres et al., 2004; Turvey, Wallace, & Herzog, 1999). Participants’ lifestyle factors included smoking status (never, former, or current) and alcohol consumption (abstainer, former, or current).

**Statistical Analysis**

Descriptive characteristics of study participants were presented as mean ±SD for continuous variables, and frequencies and proportions for categorical variables. Bivariate analyses were conducted to assess differences in participants’ sociodemographic characteristics, lifestyle factors, and health conditions by arthritis category, using chi-square test for categorical variables and t or analysis of variance tests for continuous variables. The main exposure of
interest was diagnosis of arthritis disease category, and the primary outcome variable was cognitive impairment.

A multivariable logistic regression model was used to estimate the relative odds of cognitive impairment (cognitive impaired vs. cognitive normal) with diagnosis of arthritis, adjusting for participants’ sociodemographic characteristics, health conditions, and lifestyle factors. A multinomial regression model was used to estimate the relative odds of cognitive impairment (dementia, cognitively impaired only, functionally impaired only, vs. normal group) with diagnosis of arthritis adjusting for potential covariates. Regression diagnostics were conducted for multicollinearity issues, and we did not identify correlations that warranted omission of variables. Because it is plausible that the relationship between arthritis and cognitive impairment might be influenced by other comorbid conditions, we tested for effect modification on the relationship with age, gender, and diagnosis of at least one health condition (diabetes, stroke, hypertension, heart attack, and stroke). We also tested whether depression modified the relationship between arthritis, cognitive impairment, and functional impairment by constructing models stratified according to participants’ depression status at baseline. A \( p < .05 \) was considered significant for all statistical inferences. Data management and analyses were conducted using R ver. 3.1 (R Development Core Team, 2014).

**Results**

A total of 2,681 older adults aged \( \geq 60 \) years who were neither cognitively nor functionally impaired in 2001 and who had cognitive and functional assessments in 2012 were included in the study. The average age of participants was 66.5 years (±5.4 years). Overall, 57% of older adults were females, 83% had less than 7 years of education, and 34% were not married. Approximately 12%, 39%, and 23% reported physician diagnosis of diabetes, hypertension, and depression, respectively. Approximately 14% and 29% were current smokers or current alcohol consumers, respectively. When studying characteristics by the two arthritis disease groups, approximately 48% and 35% of older adults with arthritis were hypertensive or depressed compared with 36% and 20% of those without arthritis. Approximately 70% of older adults with arthritis were female compared with 53% among those without arthritis (Table 1).

Overall, 22.7% of older adults in the cohort reported a physician diagnosis of arthritis during Wave I. Overall, 16% of the participants reported being cognitively impaired at Wave III. Approximately 8%, 9%, and 19% of older Mexican adults were categorized into the Dementia, Cognitively impaired only, or Functionally impaired only groups, respectively. Bivariate analyses
Table 1. Cohort Participants’ Baseline Sociodemographic Characteristics, Health Conditions, and Lifestyle Factors by Arthritis Diagnosis Category, Mexican Health and Aging Study, n = 2,681.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No (n = 2,076)</th>
<th>Yes (n = 605)</th>
<th>Total cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sociodemographic characteristics</strong></td>
<td></td>
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<tr>
<td>Age, years, M ±SD</td>
<td>66.3 (5.4)</td>
<td>66.8 (5.3)</td>
<td>66.5 (5.4)</td>
</tr>
<tr>
<td>Educational attainment, % (n)</td>
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</tr>
<tr>
<td>0 years</td>
<td>25.8 (535)</td>
<td>26.4 (160)</td>
<td>25.9 (695)</td>
</tr>
<tr>
<td>1-6 years</td>
<td>56.7 (1,178)</td>
<td>58.2 (352)</td>
<td>57.1 (1,530)</td>
</tr>
<tr>
<td>7+ years</td>
<td>17.5 (363)</td>
<td>15.4 (93)</td>
<td>17.0 (456)</td>
</tr>
<tr>
<td>Gender, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>46.9 (974)</td>
<td>30.2 (183)</td>
<td>43.2 (1,157)</td>
</tr>
<tr>
<td>Female</td>
<td>53.1 (1,102)</td>
<td>69.8 (422)</td>
<td>56.8 (1,524)</td>
</tr>
<tr>
<td>Marital status, % (n)</td>
<td></td>
<td></td>
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<tr>
<td>Not married</td>
<td>32.8 (680)</td>
<td>40.2 (243)</td>
<td>923 (34.4)</td>
</tr>
<tr>
<td>Married</td>
<td>67.2 (1,396)</td>
<td>59.8 (362)</td>
<td>65.6 (1,758)</td>
</tr>
<tr>
<td><strong>Health conditions</strong></td>
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<tr>
<td>Diabetes, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>88.3 (1,834)</td>
<td>86.6 (524)</td>
<td>88.0 (2,358)</td>
</tr>
<tr>
<td>Yes</td>
<td>11.7 (242)</td>
<td>13.4 (81)</td>
<td>12.0 (323)</td>
</tr>
<tr>
<td>Hypertension, % (n)</td>
<td></td>
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</tr>
<tr>
<td>No</td>
<td>63.7 (1,323)</td>
<td>51.7 (313)</td>
<td>61.0 (1,636)</td>
</tr>
<tr>
<td>Yes</td>
<td>36.3 (753)</td>
<td>48.3 (292)</td>
<td>39.0 (1,045)</td>
</tr>
<tr>
<td>Heart attack, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>97.7 (2,028)</td>
<td>97.7 (591)</td>
<td>97.7 (2,619)</td>
</tr>
<tr>
<td>Yes</td>
<td>2.3 (48)</td>
<td>2.3 (14)</td>
<td>2.3 (62)</td>
</tr>
<tr>
<td>Stroke, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>98.3 (2,041)</td>
<td>97.7 (591)</td>
<td>98.2 (2,632)</td>
</tr>
<tr>
<td>Yes</td>
<td>1.7 (35)</td>
<td>2.3 (14)</td>
<td>1.8 (49)</td>
</tr>
<tr>
<td>Depression, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>80.0 (1,660)</td>
<td>63.6 (385)</td>
<td>76.3 (2,045)</td>
</tr>
<tr>
<td>Yes</td>
<td>20.0 (416)</td>
<td>36.4 (220)</td>
<td>23.7 (636)</td>
</tr>
<tr>
<td><strong>Lifestyle factors</strong></td>
<td></td>
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<tr>
<td>Smoking, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>56.4 (1,170)</td>
<td>59.2 (358)</td>
<td>57.0 (1,528)</td>
</tr>
<tr>
<td>Former</td>
<td>29.0 (603)</td>
<td>29.4 (178)</td>
<td>29.1 (781)</td>
</tr>
<tr>
<td>Current</td>
<td>14.6 (303)</td>
<td>11.4 (69)</td>
<td>13.9 (372)</td>
</tr>
<tr>
<td>Alcohol consumption, % (n)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abstainer</td>
<td>38.2 (792)</td>
<td>40.2 (243)</td>
<td>38.6 (1,035)</td>
</tr>
<tr>
<td>Former</td>
<td>31.4 (651)</td>
<td>33.6 (203)</td>
<td>31.9 (854)</td>
</tr>
</tbody>
</table>

(continued)
did not identify a significant association of arthritis diagnosis categories with primary cognitive outcome, but a significant association with secondary outcome categories was detected \((p < .01)\). Of those older Mexican adults with arthritis, 15.5\% were cognitively impaired and 84.5\% were categorized into cognitively normal group. For those without arthritis, 16\% reported being cognitively impaired, and 84\% were cognitively normal. Of those older Mexican adults with arthritis, 8.4\% were classified as having dementia, 7.1\% reported only cognitive impairment, 28.8\% reported only functional impairment, and 55.7\% were categorized as normal. For those without arthritis, 7.1\% reported dementia, 9\% reported only cognitive impairment, 16.1\% reported only functional impairment, and 67.9\% were normal.

Table 2 presents the unadjusted and adjusted estimates of the association of arthritis with cognitive impairment (primary outcome), and with both cognitive and functional impairment (secondary outcome) among older Mexican adults. When adjusted for covariates including sociodemographic characteristics, lifestyle factors, and health conditions, compared with older adults who did not report a diagnosis of arthritis, those who reported arthritis diagnoses were 8\% (adjusted odds ratio \([OR] = 0.92, 95\% \text{ confidence interval} \,[CI] = [0.71, 1.20]) less likely to be cognitively impaired, and the point estimate was not significant. Older adults diagnosed with arthritis were more likely to be functionally impaired only \((OR = 1.82, 95\% \text{ CI} = [1.45, 2.29])\) and both functionally and cognitively impaired \((OR = 1.23, 95\% \text{ CI} = [0.86, 1.76])\) than those without arthritis, but the adjusted point estimates were significant only for relationship with functionally impaired only group.

### Table 1. (continued)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No ((n = 2,076))</th>
<th>Yes ((n = 605))</th>
<th>Total cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Arthritis at Wave I</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Current</td>
<td>30.5 (633)</td>
<td>26.3 (159)</td>
<td>29.5 (792)</td>
</tr>
<tr>
<td>Primary study outcomes at Wave III, % ((n))</td>
<td></td>
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</tr>
<tr>
<td>Cognitively normal</td>
<td>84.0 (1,743)</td>
<td>84.5 (511)</td>
<td>84.1 (2,254)</td>
</tr>
<tr>
<td>Cognitively impaired</td>
<td>16.0 (333)</td>
<td>15.5 (94)</td>
<td>15.9 (427)</td>
</tr>
<tr>
<td>Secondary study outcomes at Wave III, ** % ((n))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>67.9 (1,409)</td>
<td>55.7 (337)</td>
<td>65.1 (1,746)</td>
</tr>
<tr>
<td>Functionally impaired only</td>
<td>16.1 (334)</td>
<td>28.8 (174)</td>
<td>18.9 (508)</td>
</tr>
<tr>
<td>Cognitively impaired only</td>
<td>9.0 (186)</td>
<td>7.1 (43)</td>
<td>8.5 (229)</td>
</tr>
<tr>
<td>Dementia (both cognitively and functionally impaired)</td>
<td>7.1 (147)</td>
<td>8.4 (51)</td>
<td>7.4 (198)</td>
</tr>
</tbody>
</table>

*p < .05. **p < .01.
We did not detect an interaction of age, gender, and having at least one health condition (stroke, diabetes, hypertension, heart attack, and depression) with arthritis in risk of cognitive or functional impairment. We found that approximately 36% of older Mexican adults at baseline reported depression. We conducted stratified models by depression status and did not find substantive differences after excluding participants with depression from the fully adjusted model (cognitive impaired group: OR = 0.88, 95% CI = [0.63, 1.21]; functionally impaired only group: OR = 2.04, 95% CI = [1.54, 2.71]; cognitively impaired only group: OR = 0.99, 95% CI = [0.64, 1.53]; dementia group: OR = 1.16, 95% CI = [0.73, 1.85]).

**Discussion**

In a prospective cohort of 2,681 older Mexican adults, we found that those diagnosed with arthritis were more likely to be functionally impaired only, compared with those without diagnosis of arthritis. Similar to early studies that estimated rates of cognitive impairment and dementia in elderly Mexican populations (Ortiz et al., 2012; Velazquez-Brizuela et al., 2014), 16.3% and 7.6% of older Mexican adults in our study were identified as being cognitively impaired or having dementia. We found that older Mexican adults diagnosed with arthritis were more likely to be functionally impaired compared with those not diagnosed with arthritis. This
study finding is similar to earlier studies that reported osteoarthritis (Creamer, Lethbridge-Cejku, & Hochberg, 2000; Dominick, Ahern, Gold, & Heller, 2004; Miller, Rejeski, Messier, & Loeser, 2001; Tsai & Means, 2005) and rheumatoid arthritis (Eberhardt & Fex, 1995; Escalante, Haas, & del Rincon, 2005; Hakala, Nieminen, & Manelius, 1994) as major contributors to functional impairment or physical disability.

We did not find a significantly increased risk of cognitive impairment only or dementia among older Mexican adults with arthritis. Studies that assessed the association of rheumatoid arthritis or arthritis with risk of cognitive impairment and/or dementia have yielded mixed results. Previous reports by Jenkinson et al. (1989), McGeer et al. (1990), Broe et al. (de Jongh et al., 2011), French et al. (1985), and Breitner et al. (1994) reported decreased risk of cognitive impairment with arthritis, while studies by Heyman et al. (1984) and Wallin et al. (2012) identified increased risk. These conflicting findings might be due to differences in study designs, as most case-control studies reported decreased risk, while retrospective cohort studies reported increased risk. There is a long asymptomatic phase between the onset of neuropathological processes and the onset of cognitive impairment in cognitive disorders, and case-control studies that are retrospective inquiries might thus underestimate the impact of arthritis diagnosis due to this long asymptomatic phase, leading to decreased effect sizes. We also did not find increased risk of dementia among older Mexican adults with arthritis, unlike the study by Wallins et al. (2012), where the effect size was significant. This might be due to two decades of follow-up in the Cardiovascular Risk Factors, Aging and Incidence of Dementia (CAIDE) cohort (Wallin et al., 2012) compared with only 11 years of follow-up in the MHAS cohort, where incidence of dementia is low.

Depression during middle age has been identified as a risk factor dementia (Zilkens, Bruce, Duke, Spilsbury, & Semmens, 2014), and depressive symptoms during old age may be an early symptom of dementia (Byers & Yaffe, 2011). In addition, studies have demonstrated that older participants with depressive symptoms contribute to poor performance on cognitive assessments (Zlatar, Moore, Palmer, Thompson, & Jeste, 2014). Thus, participants included in the final sample with depressive symptoms during Wave I might be incorrectly classified as having dementia during Wave III, which may bias the reported findings. Therefore, we conducted stratified models by excluding older adults who reported depressive symptoms at Wave I from the final analytical sample, and did not detect substantial differences.

Our study exposure included older Mexican adults diagnosed with arthritis, comprising diagnoses of both osteoarthritis and rheumatoid arthritis. The possible biological mechanisms linking cognitive impairment with osteoarthritis
may be different from those linking cognitive impairment with rheumatoid arthritis. Rheumatoid arthritis is a systemic inflammatory joint disorder, and systemic inflammatory markers could possibly lead to inflammation in the brain, subsequently increasing the risk of cognitive decline and dementia (Cunningham, 2011; Cunningham & Hennessy, 2015; Dziedzic, 2006; Sundelof et al., 2009). Osteoarthritis is a degenerative joint disease, or wear-and-tear arthritis affecting the cartilage of joints, and could possibly lead to cognitive decline through associated cardiovascular events including metabolic syndrome and myocardial infarction (del Rincon, Williams, Stern, Freeman, & Escalante, 2001; Feng et al., 2013; Gami et al., 2007; Gorelick, 2010; Liu et al., 2009; Misiak, Leszek, & Kiejna, 2012; Panza et al., 2010). The questionnaire administered to participants in the MHAS cohort did not make the distinction between the two joint disorders, and might be one of the reasons for non-significant effect sizes. Also, we did not have information on non-steroidal anti-inflammatory drugs (NSAIDs) use by older Mexican adults, and studies have shown that NSAID use inhibits the cyclooxygenase enzyme, leading to marked reduction in synthesis of pro-inflammatory prostaglandins and decreased risk of cognitive decline (Cote et al., 2012; Imbimbo, Solfrizzi, & Panza, 2010). However, the biological phenomenon of this protection is not yet completely understood.

The study has limitations that merit discussion. Self-reported responses were used to define study measures and might be subject to recall bias. Our study outcomes were defined using cognitive and functional assessment measures, and misclassification bias might be possible because some participants who did not have dementia might be misclassified into the dementia group, and vice versa. In addition, our study exposure, diagnosis of arthritis, was defined using participants’ self-reported responses about physician-diagnosis arthritis and might be subject to misclassification bias as it is possible that some participants might not recall about being informed about their arthritis diagnosis by their physician, while others might misreport being informed about their arthritis diagnosis although not informed by their physicians. Because a majority of participants in our study have less than 6 years of education, it is highly likely that they might have not reported their arthritis diagnosis accurately that might have led to underestimation of the effect sizes, and future studies should address these limitations. MHAS is a prospective cohort study, and there is possibility of participants’ lost to follow-up that might influence effect sizes. Furthermore, unmeasured confounding, such as other chronic and subclinical diseases, might influence the relationship (L. Y. Chen et al., 2014; de Jongh et al., 2011; Feinkohl et al., 2013; Hadjieva & Mineva, 2010; Wijsman et al., 2013). Moreover, our cohort did not include objective measures that accurately measure arthritis and cognition decline.
(McKhann et al., 2011). Nevertheless, our study is the first study to investigate the association of arthritis with risk of cognitive and functional decline among older adults residing in Mexico.

In summary, our study findings indicate that older Mexican adults diagnosed with arthritis have significantly increased risk of functional impairment compared with those not diagnosed with arthritis. No significant association with cognitively impairment only or dementia was identified.

Declaration of Conflicting Interests
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