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Physical Activity and Associations With Computed Tomography-Detected Lumbar Zygapophyseal Joint Osteoarthritis

Pradeep Suri, MD, MS^{1,2}, David J. Hunter, MBBS, PhD³, Edward J. Boyko, MD, MPH^{1,4}, James Rainville, MD⁵, Ali Guermazi, MD, PhD⁶, and Jeffrey N. Katz, MD, MS⁷

¹VA Puget Sound Healthcare System, Seattle, WA, USA

²Department of Rehabilitation Medicine, University of Washington School of Medicine, Seattle, WA, USA

³Kolling Institute, University of Sydney and Rheumatology Department, Royal North Shore Hospital, Sydney, NSW, Australia

⁴Department of Medicine, University of Washington School of Medicine, Seattle, WA, USA

⁵New England Baptist Hospital, Boston, MA, USA

⁶Department of Radiology, Boston University School of Medicine, Boston, MA, USA

⁷Division of Rheumatology, Immunology and Allergy, Department of Medicine and Department of Orthopedic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA

Abstract

Background Context—There are no prior epidemiologic studies examining associations between physical activity and imaging-detected lumbar zygapophyseal joint osteoarthritis (ZJO) in a community-based sample.

Purpose—To determine whether physical activity is associated with prevalent lumbar ZJO on computed tomography (CT).

Study Design/Setting—Community-based cross-sectional study.

Patient Sample—424 older adults from the Framingham Heart Study.

Outcome Measures—Participants received standardized CT assessments of lumbar ZJO at the L2-S1 levels. Severe lumbar ZJO was defined according to the presence and/or degree of joint space narrowing, osteophytosis, articular process hypertrophy, articular erosions, subchondral cysts, and intraarticular vacuum phenomenon. This definition of lumbar ZJO was based entirely on CT imaging findings, and did not include any clinical criteria such as low back pain.

Corresponding Author: Pradeep Suri MD MS; VA Puget Sound Healthcare System; 1660 S. Columbian Way, RCS-117; Seattle, WA 98108; tel: 206-764-1812; fax: 206-764-5613; pradeep.suriyaarachchi@va.gov.

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Methods—Physical activity was measured using the Physical Activity Index, which estimates hours per day typically spent in these activity categories: sleeping, sitting, slight activity, moderate activity, or heavy activity. Participants reported on usual frequency of walking, running, swimming, and weightlifting. We used multivariable logistic regression to examine associations between self-reported activity and severe lumbar ZJO, while adjusting for key covariates including age, sex, height, and weight. Study funding was from NIH-K12HD01097. There were no study-specific conflicts of interest-associated biases.

Results—In multivariable analyses, ordinal categories of heavy physical activity duration per day were significantly associated with severe lumbar ZJO (p for trend=0.04), with the greatest risk observed for the category ≥ 3 hours/day (odds ratio [OR] 2.13 (95% confidence interval [CI]): 0.97–4.67). When heavy activity was modeled as a continuous independent variable, each hour was independently associated with 1.19 times the odds of severe lumbar ZJO (95% CI 1.03–1.38; $p=0.02$). Less vigorous types of physical activity and the type of exercise were not associated with severe lumbar ZJO. Older age, lesser height, and greater weight were independently and significantly associated with severe lumbar ZJO. In multivariable models predicting lumbar ZJO, neither model discrimination nor reclassification improved with the addition of physical activity variables, as compared to a multivariable model including age, sex, height, and weight.

Conclusions—Our findings demonstrate a statistically significant cross-sectional association between heavy physical activity and CT-detected severe lumbar ZJO. However, the additional discriminatory capability of heavy physical activity above and beyond that contributed by other factors was negligible.

INTRODUCTION

The lumbar zygapophyseal (or ‘facet’) joints are a commonly treated source of back pain in the United States [1]. Lumbar zygapophyseal joint osteoarthritis (ZJO) is thought to be a potential cause of low back pain in instances where pain can be isolated to the zygapophyseal joints using diagnostic anesthetic blocks [2]. Population-based epidemiologic studies have identified several potential risk factors for imaging-detected lumbar ZJO, including older age, female sex, and obesity [3, 4]. No studies to date have examined associations between lumbar ZJO on diagnostic imaging and physical activity exposures such as general physical activity or performance of leisure-time exercise or sports [4].

The effects of physical activity on spinal degeneration and low back pain are complex, and our understanding of the interrelationships between these factors continues to evolve [5–7]. The magnitude of associations between spinal degeneration (spondylosis) in the lumbar intervertebral discs and zygapophyseal joints and low back pain, when present, is relatively modest [8, 9]. Physical activity is generally thought to have beneficial effects on the severity of low back pain, and therapeutic exercise is a standard-of-care conservative treatment for nonspecific back pain [10–12]. On the other hand, views on the effects of physical activity on spinal degeneration are mixed, with both positive and negative putative effects attributed to physical activity [6, 13–15]. The effects of physical activity on spinal degeneration may be dependent on the type, intensity, and cumulative exposure of the specific physical activity involved. Of note, well-designed studies of lumbar disc degeneration have illustrated that deleterious effects of physical activity on prevalent and incident lumbar disc degeneration

are small in magnitude, when present at all [6, 16, 17]. These facts underscore the need for better understanding of the role of physical activity in spinal degeneration. To date, all epidemiologic research in this area has examined putative effects of physical activity on the intervertebral discs, without consideration of effects on the lumbar zygapophyseal joints.

We conducted a study to examine cross-sectional associations between physical activity and computed tomography(CT)-detected lumbar ZJO in a sample of community-based US adults. The aim of this study was to determine whether general physical activity or specific types of exercise are associated with prevalent lumbar ZJO, when adjusting for demographic factors, and potential contributions to physical loading from anthropometric factors. For the purposes of this manuscript, the term 'ZJO' refers specifically to CT-detected zygapophyseal joint osteoarthritis, irrespective of clinical symptoms such as low back pain, which were not evaluated in this study.

MATERIALS AND METHODS

Study Participants

This ancillary study to the Framingham Heart Study was approved by the Institutional Review Board of New England Baptist Hospital. The Offspring cohort of the Framingham Heart Study was initiated in 1971 as a prospective epidemiologic study of 5124 young adults [18]. The Generation 3 cohort was established in 2002, and included 4095 adults who were children of the Offspring cohort members [19]. 3529 participants from the Offspring and Generation 3 cohorts underwent abdominal computed tomography (CT) scanning to assess abdominal aortic calcification, as described in detail elsewhere [20, 21]. These scans also underwent standardized imaging evaluations for features of lumbar spondylosis, including lumbar ZJO. Subjects for this ancillary investigation were randomly selected from amongst those individuals within the CT cohort, on the basis of randomly generated numbers. The Offspring cohort was oversampled to enrich the sample for older adults with a greater prevalence of severe spinal degeneration. Physical activity and covariate data were taken from the scheduled Framingham clinical examinations that best corresponded temporally with the timing of the CT scans (Examination 8 for the Offspring participants, and Examination 1 for the Generation 3 participants); the CT scans were obtained an average of 1 year before the clinical examination.

Assessment of Physical Activity and Exercise

Measures of physical activity were drawn from the Framingham Physical Activity Index, an interviewer-administered questionnaire that measures metabolic work done during a typical day [22].

1. **Physical Activity Categories:** The Physical Activity Index estimates how many hours per day participants typically spend in the following physical activity categories: 1) sleeping (h_{sleep}), 2) sitting ($h_{\text{sedentary}}$), 3) slight activity(h_{slight}), 4) moderate activity(h_{moderate}), and 5) heavy activity(h_{heavy}). Trained interviewers provided examples of slight, moderate, and heavy activities, which could include activities performed at work, in the home, or during leisure-time sports or other activities. Slight activities included those such as standing or normal walking, and

light household activities such as ironing. Moderate activities included those such as brisk walking, lifting or carrying light objects, and moderate household activities such as sweeping and vacuuming. Heavy activities included those such as jogging, brisk bicycling, or other strenuous recreational or sports activities, lifting and/or carrying objects heavier than 5 pounds, and heavy household tasks such as lawn-mowing, shoveling, digging, or chopping wood.

2. **Continuous-scaled Physical Activity:** The items from the Physical Activity Index were combined as a continuous-scaled *Activity Score* which estimates daily oxygen consumption [23]: $\text{Activity Score} = (1.0 \times h_{\text{sleep}}) + (1.1 \times (h_{\text{sedentary}})) + (1.5 \times (h_{\text{slight}})) + (2.4 \times (h_{\text{moderate}})) + (5.0 \times (h_{\text{heavy}}))$. This Activity Score has been validated as a predictor of incident all-cause and cardiovascular mortality [23]. Since the continuous Activity Score has little intrinsic meaning, we dichotomized this variable for analytic purposes. We created two dichotomous variables, one with a predefined cutpoint at the 50th percentile, and the other with a cutpoint at the 75th percentile.
3. **Specific Types of Exercise:** Participants were also asked to report their usual frequency of performing specific types of exercise, including walking for exercise or walking to work, running/jogging, weight training, and swimming. Reported frequency of performing these types of exercise was grouped in categories of average minutes/hours spent per week in the activity.

Assessment of Anthropometric Factors and Other Covariates

Trained examiners conducted measurements of height and weight at each clinical examination. Body mass index (BMI) was calculated as weight (converted into kilograms) divided by the square of height (converted into meters). Data were also collected on participant age, and participant-reported sex and race.

Assessment of Lumbar Zygapophyseal Joint Osteoarthritis

CT assessments were performed using eFilm Workstation (Version 2.0.0, Merge Healthcare, Milwaukee, USA) software. Lumbar ZJO was graded at the left and right zygapophyseal joints of spinal levels L2-L3, L3-L4, L4-L5, and L5-S1. OA severity was graded using the Framingham Scale, a semi-quantitative measure which assesses the presence and extent of characteristics such as joint space narrowing, osteophytosis, articular process hypertrophy, sclerosis, subarticular erosion, subchondral cystic change, and presence of vacuum phenomenon [24]. We selected the presence of severe lumbar ZJO as our study outcome, based on earlier work demonstrating this threshold of severity to be associated with back pain in Framingham older adults [9], in advance of any analyses conducted for this study. Severe lumbar ZJO was defined as the presence of marked or total joint space narrowing, and/or large osteophytes; and/or severe articular process hypertrophy; and/or severe articular erosions; and/or severe subchondral cysts; and/or joint space vacuum phenomenon. All CT assessments were performed with blinding to clinical information by a board-certified, fellowship-trained nonoperative spine physiatrist (PS), who was trained by a musculoskeletal radiologist (AG). The physiatrist reader calibrated to the radiologist prior to the start of formal reads using training sets of CT scans, and recalibration was repeated

during the reading process. A reference atlas for lumbar ZJO was used throughout the study. Inter-observer reliability between the physiatrist and radiologist was reassessed periodically in order to evaluate for reader-drift. Reliability using the weighted κ statistic ranged between 0.68 and 0.84 for lumbar ZJO, which represents moderate to excellent reproducibility.

Statistical analysis

We descriptively characterized the sample with respect to sociodemographics, anthropometrics, and lumbar ZJO. We then created a 'core' multivariable logistic regression model predicting severe lumbar ZJO that included age, sex, and anthropometrics as independent variables. To select covariates for inclusion in the core model, we tested different combinations of anthropometric factors, including the variables of height, weight, and BMI (both separately and in combination), in order to utilize the most parsimonious combination of variables. We compared models with respect to model discrimination as reflected by the c -statistic, and model fit using the Akaike Information Criterion. This approach was taken in order to account for the possibility that the specific quadratic height-weight interrelationship indicated by BMI (weight/height^2) might not have relevance in the setting of lumbar ZJO. Once the most parsimonious core model was selected, we then added individual physical activity variables to the core model, in order to examine independent associations between physical activities and severe lumbar ZJO. This resulted in a series of separate multivariable models where only one activity variable was adjusted for at a time. These physical activity variables consisted of 1) *physical activity categories*, 2) *Activity Score variables*, and 3) *specific types of exercise* (walking for exercise/walking to work, running/jogging, weight training, and swimming). Physical activity categories were analyzed both as continuous and ordinal variables, with cutpoints for the latter chosen to maximize cell counts within four separate strata. For those physical activity variables with statistically significant independent associations with lumbar ZJO, we examined changes in model discrimination before and after addition of physical activity variables to the core multivariable model, using the c -statistic. Due to potential insensitivity of the c -statistic in assessing the impact of adding new predictors to a multivariable model, we also examined the ability of physical activity variables, when added to the core multivariable model, to correctly reclassify individuals within tertiles of predicted lumbar ZJO risk. To do this, we calculated net reclassification improvement using the Net Reclassification Index (NRI) [25]. For subjects with lumbar ZJO, the NRI counts the proportion of participants moving to a higher tertile of ZJO predicted risk, minus the proportion that move to a lower tertile. Similarly, for subjects without lumbar ZJO, the NRI counts the proportion moving to a lower tertile of ZJO predicted risk, minus the proportion that move to a higher tertile. The NRI is the sum of these two components [26]. We performed subgroup analyses to examine whether associations between physical activity and lumbar ZJO were different according to age, sex, height, weight, or BMI. Where differential effects were seen between subgroups, we tested for statistical interactions by inclusion of interaction terms in the multivariable models. Analyses were performed using SPSS software, version 20.0.0 (IBM Corporation, Armonk, NY) and STATA version 13.0 (College Station, Texas).

RESULTS

Four hundred twenty four participants comprised the study sample (Table 1). The mean age of participants was 59.4 ± 12.1 years and approximately half were female. Participants were overweight on average with a mean BMI of 27.9 ± 5.0 kg/m² [27]. Thirty four percent of participants had one or more lumbar zygapophyseal joints with severe OA at the L2-S1 spinal levels.

The ‘core’ multivariable model included age (odds ratio [OR] 1.08 per year; 95% confidence interval [CI] 1.05–1.10), female sex (OR 1.05 [95% CI 0.53–2.07]), height (OR 0.86 per inch [95% CI 0.77–0.95] and weight (OR 1.01 per pound [95% CI 1.01–1.02]), with a model *c* statistic of 0.787. This combination of variables optimized both model discrimination and model fit, as compared to other multivariable models, with or without inclusion of BMI as a covariate (data not shown). Table 2 presents multivariable-adjusted associations between self-reported physical activities and severe lumbar ZJO, when adjusting for age, sex, height, and weight. The number of daily hours spent in heavy physical activity, when treated as an ordinal variable, was independently and significantly associated with the presence of severe lumbar ZJO (Table 2). The relative odds of severe lumbar ZJO with 3 hours/day of heavy physical activity compared to 0 hours/day of heavy physical activity was 2.13 (95% CI 0.97–4.67). When heavy physical activity was treated instead as a continuous variable (number of hours/day), each hour of activity was associated with 1.19 times the odds of severe lumbar ZJO (95% CI 1.03–1.38; *p*=0.02), independent of other factors. Significant associations with severe lumbar ZJO were not seen for moderate or slight physical activity or sitting whether coded as ordinal (Table 2) or continuous variables (data not shown). The Activity Score was not associated with severe lumbar ZJO when dichotomized at the 50th percentile, however, the 75th percentile cutpoint was associated with lumbar ZJO (OR 1.73 [95% CI 1.02–2.92; *p*=0.04]) compared to the lower 3 quartiles. Specific leisure-time activities were not significantly associated with severe lumbar ZJO. In sensitivity analyses adjusting for BMI instead of height and weight separately, multivariable-adjusted associations between heavy physical activity as a continuous variable (OR 1.19 per hour, per day [95% CI 1.03–1.38; *p*=0.02), or Activity Score dichotomized at the 75th percentile (OR 1.79 [95% CI 1.06–3.02; *p*=0.03]), and lumbar ZJO were essentially unchanged.

When examining the incremental improvement in model discrimination by adding physical activity variables to the core model, the greatest increase was seen for the addition of heavy physical activity (either as an ordinal variable or as a continuous variable), and for Activity Score dichotomized at the 75th percentile. However, increases in the *c* statistic conferred by the addition of these variables were quite small (0.005 for heavy physical activity whether ordinal or continuous, and 0.007 for Activity Score at 75th percentile cutpoint). Furthermore, the addition of these physical activity variables did not materially result in improved reclassification of lumbar ZJO compared with the core multivariable model, and changes in the NRI were not statistically significant (data not shown).

In subgroup analyses, stratification of the sample at the median age (57 years), demonstrated that the magnitude of the multivariable-adjusted association between heavy physical activity and severe lumbar ZJO was significantly greater in younger adults (Table 3). In

multivariable models including interaction terms for age x heavy activity, there were statistically significant interactions between age (<57 years vs. ≥57 years) and the number of hours/day of physical activity in the prediction of lumbar ZJO ($p=0.02$), and between age and ordinal categories of heavy physical activity ($p=0.02$). There were no statistically significant interactions between heavy physical activity and sex, height, weight, or BMI in the prediction of lumbar ZJO (data not shown).

DISCUSSION

Self-reported daily heavy physical activity, and the upper quartile of estimated daily oxygen consumption as measured by the Activity Score, were significantly and independently associated with prevalent severe lumbar ZJO in this sample of community-based US older adults. However, consideration of these physical activity variables did not meaningfully increase the ability to discriminate between individuals with and without severe lumbar ZJO, beyond the explanatory value provided by age, sex, height, and weight. Furthermore, consideration of these physical activity variables did not significantly improve classification according to tertiles of predicted ZJO risk. These results are suggestive of an overall effect of physical activities on CT-detected lumbar ZJO that is small to minimal, when other factors are taken into account.

Although to our knowledge this is the first study examining associations between physical activity and lumbar ZJO, our findings are consistent with those of earlier studies examining the association of physical activity with the related spondylosis feature of disc degeneration. The Finnish Twin Spine Study utilized highly precise quantitative measures of lumbar disc degeneration (disc height and disc desiccation), and found that occupational and leisure-time physical activities explained a statistically significant but relatively minor portion of the overall variance in lumbar disc degeneration [28]. Videman et al. hypothesized that anthropometric factors, which in theory may load the spine continuously during all daily activities, might have greater effect on disc degeneration than the specific effects of ‘external’ loading during tasks such as lifting or bending. This was confirmed in analyses which demonstrated absent or small magnitude cross-sectional associations between occupational and leisure-time physical activities and disc degeneration, and a negligible proportion of additional variance explained when the most significant occupational activities were added to multivariable models including age, anthropometrics, and/or lifting strength [6].

Of note, our study found that only heavy physical activities, or the highest quartile of estimated daily oxygen consumption associated with overall physical activity, showed associations with lumbar ZJO. Given the relative weight (~5-fold) placed on heavy activity in the calculation of the continuous Activity Score, the association with its highest quartile is likely to be driven largely by the contribution of heavy activity. However, the grouping of multiple activity types under the category ‘heavy’ in the Framingham Physical Activity Index limits our understanding of which *specific* activities are most strongly associated with lumbar ZJO. Sitting has been proposed as a possible cause of mechanical stress to the zygapophyseal joints [29], but we detected no association with lumbar ZJO for sitting, nor were associations seen with walking, running, or swimming. The non-significant trend noted

towards a higher prevalence of lumbar ZJO in those individuals with high weight lifting exposures ~2 hours/week (Table 2) might suggest that lifting and bending exposures explain the association of self-reported heavy activities with lumbar ZJO, but this speculation would require further examination in studies using higher resolution activity measures which specify particular actions or tasks. Another interesting finding of this study was the fact that heavy activity was independently associated with lumbar ZJO in younger adults, but not in older adults. Although this might reflect a biologic relationship wherein mechanical loading has smaller effects in older joints than younger joints, this would appear inconsistent with the general view that the capacity of load-bearing synovial joints to adapt to mechanical stress decreases with age. A more likely explanation would be the large magnitude effect of age (and as yet unidentified factors) on lumbar ZJO, such that adults with a predisposition to ZJO have already developed it by later life, limiting the potential for any additional contribution attributable to heavy activity.

A important strength of the current study is the community-based sample, in contrast to most prior studies of ZJO which have been conducted in clinical convenience samples [4]. Study limitations include the cross-sectional design, which limits conclusions regarding temporality, and cannot accurately distinguish causes of lumbar ZJO from consequences. Since our findings present the first report of a significant association between heavy physical activity and ZJO on diagnostic imaging, based on only 12% of the Framingham CT cohort participants, future studies are needed to confirm this result in other samples. Such studies would benefit from a longitudinal design to elucidate temporality and the role of possible mediating factors such as low back pain, which we did not examine in this study. Indeed, one could imagine a scenario where individuals with severe lumbar ZJO are more likely to have low back pain, and may decrease their activity levels due to having pain. This might have obscured real associations between physical activities and ZJO in our study, or have resulted in a downward bias for our estimate of the association with heavy physical activity. Future studies might also benefit from the use of more refined activity measures, to better ascertain which specific heavy physical activities (if any) convey an increased risk of lumbar ZJO, and what the magnitude of these effects are. An ideal activity measure would categorize activities not only according to metabolic expenditures (such as the Framingham Physical Activity Index), but also according to the magnitude of mechanical stress imparted on the lumbar spine. Physical activity is an extremely important area of inquiry, since maintaining physical activity is considered a key lifestyle intervention for patients with low back pain [11], and physical activity moreover has a host of other benefits outside of the musculoskeletal system, including clear positive effects on cardiovascular and all-cause mortality [23, 30, 31]. Although risk factors for structural/anatomic changes in the lumbar spine are often presumed to be risk factors for low back pain, it is possible that heavy physical activity might have some detrimental structural effects on the lumbar zygapophyseal joints, alongside beneficial (protective) effects related to the production of low back pain, via changes in pain processing or modulation, or the behavioral aspects of pain. Last, future epidemiologic studies may also benefit from simultaneously assessing different structural outcomes such as ZJO and disc degeneration, along with clinical outcomes such as low back pain, in order to better examine the interrelationship of posterior and anterior spinal structures thought to be instrumental in producing spinal instability and

low back pain [32]. Ideally, such studies would adjust for a wide range of potential confounders such as smoking, physical trauma, and occupational factors [24].

In conclusion, our findings demonstrate a statistically significant cross-sectional association between heavy physical activity and severe ZJO. Older age, lesser height, and greater body weight were also associated with severe ZJO; the additional discriminatory capability of heavy physical activity above and beyond that contributed by these factors was negligible. Longitudinal studies are needed to confirm these findings and determine whether specific tasks, actions, and types of exercise confer greater risk of ZJO.

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Table 1

Study Sample (n=424)

	n (%) or mean (SD) *
Sociodemographics	
Age (yrs.)	56.9 (12.9)
Female Sex	195 (46.0%)
White Race	418 (98.6%)
Anthropometric Factors	
Height (inches)	66.8 (3.8)
Weight (pounds)	177.3 (38.0)
Body Mass Index (kg/m ²)	27.9 (5.0)
Lumbar Zygapophyseal Joint Osteoarthritis (ZJO)	
Any Moderate Lumbar ZJO	293 (69.1%)
Any Severe Lumbar ZJO	144 (34.0%)

* n=number, SD= standard deviation

Table 2

Multivariable-Adjusted Associations between Self-reported Physical Activities and Lumbar Zygapophyseal Joint Osteoarthritis* (n=424)

	Adjusted Odds Ratio (95% CI)	p-value
Physical Activity Categories (hours per day)		
Heavy Activity		
0 hours (reference)	1.0	
1 hours	1.58 (0.91–2.5)	
2 hours	1.52 (0.66–3.47)	
3+ hours	2.13 (0.97–4.67)	0.04[†]
Moderate Activity		
0–1 hours (reference)	1.0	
2–3 hours	0.75 (0.37–1.51)	
4–5 hours	1.19 (0.59–2.41)	
6+ hours	1.23 (0.57–2.69)	0.25 [†]
Slight Activity		
0–2 hours (reference)	1.0	
3–4 hours	0.83 (0.41–1.68)	
5–6 hours	0.75 (0.37–1.54)	
7+ hours	0.70 (0.33–1.47)	0.33 [†]
Sitting		
0–4 hours (reference)	1.0	
5–6 hours	1.17 (0.60–2.30)	
7–8 hours	1.34 (0.69–2.58)	
9+ hours	0.85 (0.45–1.62)	0.70 [†]
Activity Score (hours per day)		
Top 50 th percentile (34.7)	1.23 (0.77–1.96)	0.39
Top 25 th percentile (38.4)	1.73 (1.02–2.92)	0.04
Specific Types of Exercise (hours per day)		
Walking (for exercise or walking to work)		
Any walking	1.32 (0.71–2.43)	0.38
Regular walking (60+ mins per week)	1.05 (0.64–1.72)	0.84
Regular walking (120+ mins per week)	1.05 (0.65–1.69)	0.85
Jogging or Running (Any)	1.06 (0.45–2.45)	0.90
Swimming		
Any swimming	0.69 (0.38–1.24)	0.21
Regular swimming (60+ mins per week)	0.92 (0.45–1.89)	0.82

	Adjusted Odds Ratio (95% CI)	p-value
Regular swimming (120+ mins per week)	0.52 (0.19–1.42)	0.20
Weight training		
Any weights	1.08 (0.65–1.82)	0.76
Regular weights (60+ mins per week)	1.52 (0.84–2.76)	0.17
Regular weights (120+ mins per week)	1.96 (0.89–4.31)	0.10

* Results of separate multivariable models for the association of each activity type with severe lumbar zygapophyseal joint osteoarthritis, adjusting for age, sex, height, and weight. Only one activity variable was adjusted for in each multivariable model.

[†] p-value for trend; significant p-values 0.05 in bold

Table 3

Age-Specific Multivariable-Adjusted Associations between Self-reported Physical Activities and Lumbar Zygapophyseal Joint Osteoarthritis* (n=424)

	Younger (<57 years)		Older (≥ 57 years)	
	Adjusted Odds Ratio (95% CI)	p-value	Adjusted Odds Ratio (95% CI)	p-value
Heavy Physical Activity in a Typical Day				
Number of Hours	1.28 (1.04–1.56)	0.02	0.99(0.78–1.26);	0.95
Categories of Activity				
0 hours (reference)	1.0		1.0	
1 hours	1.75 (0.59–5.17)		1.45 (0.74–2.85)	
2 hours	2.32 (0.69–7.81)		0.77 (0.23–2.58)	
3+ hours	3.94 (1.12–13.85)	0.03[†]	1.20 (0.43–3.36)	0.74 [†]

* Dichotomized at 50th Percentile for age (<57 years vs. age ≥ 57 years), adjusted for sex, height, and weight within age strata; significant p-values 0.05 in bold