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HEIGHT AND RADIOGRAPHIC OSTEOARTHRITIS: AN EPIDEMIOLOGIC ASSESSMENT — SHORT COMMUNICATION

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ABSTRACT

Purpose: To epidemiologically assess the gender-specific relationship between height and radiographic osteoarthritis (OA) of the knee, hand, foot, and cervical spine. **Methods:** Data collected from men ($N = 1090$) and women ($N = 2441$) aged 40 years and older participating in the Clearwater Osteoarthritis Study (1988–current) were used ($N = 3531$). Physical exams including radiographs were conducted. The Kellgren and Lawrence ordinal scale was used to determine evidence of radiographic OA. **Results:** There is a modest, albeit consistent, increase in OA prevalence among shorter-stature study subjects at all four sites in women and at two sites in men (hands and cervical spine). Our adjusted findings suggest that shorter stature is a risk factor for OA for the hands, feet, and cervical spine, with odds ratios varying between 1.25 and 1.82. After adjusting for body mass index and age, this relationship maintained statistical significance among women for hand OA. (OR $= 1.57; p = 0.0001$) and feet OA (OR $= 1.41; p - value = 0.009$). Curiously, no significant association was indicated between height and knee OA for either gender. **Conclusions:** Shorter stature appears to be associated with an elevated risk of OA, but particularly so for women. Future epidemiologic studies examining this relationship can offer insight into skeletal growth and development knowledge, thus further elucidating the etiology of OA.

Keywords: Arthritis; Genetics; Stature; Skeletal growth; Risk.

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INTRODUCTION

Recent data from the National Human Genome Research Institute (NHGRI) suggest that understanding the factors involved in human height may provide new insights into osteoarthritis (OA) and other musculoskeletal diseases. GDF5 is a protein involved in the development of cartilage and may play a specific function in the etiology of OA.[4] A 2008 genetic study indicated that common variants in the OA-associated locus GDF5 contribute to variation in height.[5] This study indicated that there may be an association between short stature and an elevated risk of OA. Sanna *et al*.[5] suggested that the link between the genetic basis of height and OA could be potentially mediated through alterations in bone growth and development. It is speculated that genetic variants that reduce the production of the GDF5 protein may affect the amount of cartilage in the spine, the proportion of limbs, and/or the angles of joints, resulting in both decreased height and increased susceptibility to OA. In this brief communication, we report findings from an epidemiologic assessment of the relationship between height and site-specific OA.

METHODS

Our study's primary null hypothesis was that there was no association between height and risk of OA. We used data from the Institutional Review Board (IRB)-approved Clearwater Osteoarthritis Study (COS), which was initiated in 1988 by The Arthritis Research Institute of America (ARIA). The COS is an ongoing community-based, longitudinal cohort study designed to identify the major risk factors for the development and progression of radiographic OA. Currently in its 20th year, the 25-year longitudinal study follows individuals 40 years of age and older, collecting demographic, historical, clinical, and radiological data. The COS houses one of the world's largest repositories of sequential OA radiographs.

After eligibility was determined and written informed consent was obtained, participants completed the COS History Questionnaire. The following study subjects were excluded from enrollment: individuals with self-reported rheumatoid arthritis or variants (lupus erythematosus, ankylosing spondylitis, etc.), gout, or disabling neuralgic disease; those confined to a wheelchair; and those not able to give consent. Study participants were re-evaluated biennially, updating both the clinical, history and radiographic information.

The study exposure variable was height (m). Height was measured in stocking feet. The study outcome was site-specific radiographic OA of the knee, hand, foot, and cervical spine. A licensed X-ray technician using standard exposure techniques took hand, lateral cervical spine, and anteroposterior weight-bearing knee and weight-bearing foot radiographs. A board-certified radiologist, blinded to study subjects' information, interpreted all of the radiographs in the same manner. The Kellgren and Lawrence[2] scale was used with OA disease defined as grade 2+. The six bilateral hand joints assessed were the second distal interphalangeal (DIP) joint, third proximal interphalangeal (PIP) joint, and first carpometacarpal (CMC) joint. Foot OA status was based on radiological evidence of disease in the first metatarsophalangeal (MTP) joint. Analyses are presented by gender.

Statistical Analyses

Descriptive baseline data were generated through the calculation of frequencies and means. Our study objective was to evaluate the risk of radiographic OA by height. We report gender-specific odds ratios (ORs) between the lowest and highest height tertiles for each site. Although two-sample

t-tests were run (with significant results), reporting an estimate of the degree of disease risk (i.e. ORs) offers a better measure of the strength of this association. The factors in our adjusted statistical model were height, BMI, and age. Results from the crude and adjusted analyses are reported. Statistical Analysis Software (SAS) Version 9.2 was used for all analyses.

RESULTS

Our study sample consisted of 69% women. The subjects' age categories of <60 years, 60–74 years, and 75+ years were 42%, 46%, and 12%, respectively. The percentage of subjects with OA differed by site with knee, hand, foot, and C-spine percentages of 17%, 42%, 20%, and 28%, respectively.

Some studies, either epidemiologic or genetic, suggest that short stature is associated with an elevated risk of OA. Some reports have intimated that this association may be present at both ends of the height scale. Thus, our initial exploratory analyses utilized our large sample size by examining site-specific disease prevalence, by height, in deciles. These data displayed no evidence of a U- or J-shaped risk curve for any of the four sites investigated. Consequently, we divided our gender-specific height distributions into tertiles (Table 1). As can be seen in this table, there is a modest, albeit consistent, increase in OA prevalence among shorter-stature study subjects at all four sites in women and at two sites in men (hand and cervical spine).

We further assessed the association between height and OA by computing gender-specific ORs between the lowest and highest tertiles for each site (Tables 2 and 3). In our study sample, shorter-stature as a risk for OA is consistently evidenced for the hands, feet, and cervical spine, with crude ORs varying between 1.35 and 1.82. In our unadjusted analyses, only the knee OR for men is not above the null value of 1.0. After adjusting for

Table 1 Height Tertiles (%) Among Those with Site-Specific Osteoarthritis (OA).

	Knee OA	Hand OA	Foot OA	C-spine OA
Women only				
Low	17.5	49.8	21.4	30.0
Moderate	16.3	42.9	16.9	26.9
High	14.1	35.3	14.8	24.1
Men only				
Low	17.0	45.1	26.1	35.1
Moderate	20.7	42.5	27.8	32.2
High	17.5	36.4	19.5	26.6

Table 2 Odds Ratios Between Low and High Height Tertiles by Site-Specific OA for Women Only.

	Knee OA		Hand OA		Foot OA		C-spine OA	
	Yes	No	Yes	No	Yes	No	Yes	No
Low	140	658	400	403	170	624	239	558
High	122	742	307	563	128	736	208	654
Odds ratio	1.29		1.82		1.57		1.35	
p-value	0.06		0.0001		0.001		0.008	
95% C.I.	0.99–1.69		1.50–2.21		1.22–2.02		1.08–1.67	
Adjusted OR	0.97		1.57		1.41		1.18	
p-value	0.83		0.0001		0.009		0.16	
95% C.I.	0.74–1.28		1.28–1.93		1.09–1.83		0.94–1.47	

C.I.: confidence interval.

Table 3 Odds Ratios Between Low and High Height Tertiles by Site-Specific OA for Men Only.

	Knee OA		Hand OA		Foot OA		C-spine OA	
	Yes	No	Yes	No	Yes	No	Yes	No
Low	54	263	144	175	83	235	110	203
High	51	240	107	187	57	236	77	213
Odds ratio	0.97		1.44		1.46		1.50	
p-value	0.92		0.03		0.05		0.03	
95% C.I.	0.64–1.47		1.04–1.99		1.00–2.14		1.06–2.12	
Adjusted OR	0.82		1.25		1.29		1.32	
p-value	0.38		0.20		0.20		0.13	
95% C.I.	0.53–1.27		0.89–1.75		0.87–1.92		0.92–1.90	

body mass index and age, this relationship maintained statistical significance among women for hand OA (OR = 1.57; p = 0.0001) and feet OA (OR = 1.41; p-value = 0.009). Although shorter stature men continued to show an elevated risk of hand, foot and cervical spine OA, consideration of BMI and age attenuated the strength and significance of this association (Tables 2 and 3). The strongest association between height and radiographic OA was observed in the hand among women (OR = 1.57; p-value = 0.0001).

DISCUSSION

Our study cohort is a nonrandom sample from communities in or near Clearwater, FL. Generalizability to the surrounding community may be limited based on study recruitment design. A potential bias in our cohort is an oversampling of those persons interested in OA, thus possibly artificially elevating the prevalence of this disease in our cohort. Despite this potential generalizability limitation, important findings have been forthcoming from the COS data and other similarly collected cohort data sets. The potential bias introduced into our data would be of concern if estimating disease prevalence; however, we believe that our population is appropriate for estimating associations or disease risk.

A study strength is the objective measurement of radiographic OA using the Kellgren and Lawrence ordinal scale. Radiographs were read blindly using a carefully controlled method. In addition to the consistency of disease status measurement, our cohort sample size affords an appropriate amount of statistical power for estimating category-specific risk estimates.

Our study's primary null hypothesis was that there was no association between height and risk of OA. However, gender-stratified analyses showed that for three sites examined (hand, foot, and C-spine), women demonstrated an association between height and OA. Although it did not achieve statistical significance, men showed a similar association at all sites except the knee. Our findings suggest that shorter stature is associated with an elevated risk for radiographic OA, particularly so for women. In accord with recent suggestions generated from genetic studies, the results seen in this brief report support the contention that short stature alone is associated with an increased risk of OA. The relationship between stature and OA has been investigated in association with diseases such as familial osteochondritis.[6] Our current epidemiologic study adds insight into an association previously suggested through genetic studies.[1,3,7] As a cornerstone of epidemiologic inquiry, replication of results from varying populations is encouraged.

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