

Published in final edited form as:

Arthritis Rheum. 2013 February ; 65(2): 373–377. doi:10.1002/art.37775.

Differences in Multi-joint Symptomatic Osteoarthritis Phenotypes by Race and Gender: The Johnston County Osteoarthritis Project

Amanda E. Nelson, MD, MSCR¹, Yvonne M. Golightly, PT, PhD^{1,2}, Jordan B. Renner, MD^{1,3}, Todd A. Schwartz, DrPH^{1,2}, Virginia B. Kraus, MD, PhD⁴, Charles G. Helmick, MD⁵, and Joanne M. Jordan, MD, MPH¹

¹Thurston Arthritis Research Center, University of North Carolina, Chapel Hill, NC

²Gillings School of Global Public Health, University of North Carolina, Chapel Hill, NC

³Department of Radiology, University of North Carolina, Chapel Hill, NC

⁴Duke University Medical Center, Durham, NC

⁵Centers for Disease Control and Prevention, Atlanta, GA*

Abstract

Objective—To determine race and gender differences in phenotypes (patterns) of multiple joint symptomatic osteoarthritis (sOA) involvement.

Methods—We performed a cross-sectional analysis of sOA phenotypes in a community-based cohort, for those with sOA data for the hands, knees, hips, and lumbosacral spine (LS) collected at a single visit (2003–10). Mutually exclusive phenotypes describing all combinations of these 4 sites were compared using Fisher exact tests. For phenotypes occurring in more than 40 persons, logistic regression adjusted for race, gender, age, and body mass index (BMI) was performed and interactions by race and gender were assessed.

Results—The sample included 1650 participants, 36% men, 32% African American, with a mean age of 66 years and BMI 31 kg/m². Overall, 13% had hand, 25% knee, 11% hip, and 28% had LS sOA. African Americans compared with Caucasians were less likely to have Hand Only or in some combination, but more likely to have Knee Only. Men compared to women were less likely to have Hand Only, but more likely to have LS Only.

Conclusions—There are differences in phenotypes of multiple joint sOA involvement by race and gender that may influence definitions of multiple joint, or “generalized” OA.

Although multiple joint sites are often involved in osteoarthritis (OA) (1–4), there is no accepted definition of “generalized OA.” We have identified differences by race in phenotypes of radiographic OA (rOA) in individual joints: for instance, African Americans compared with Caucasians have more osteophytes in the knee and hip (5, 6); in addition, African Americans have different patterns of multiple joint rOA including more knee and

Corresponding Author: Amanda E. Nelson, MD, MSCR, Thurston Arthritis Research Center, University of North Carolina at Chapel Hill, 3300 Doc J. Thurston Building CB#7280, Chapel Hill, NC 27599 Phone (919)966-0553; fax (919)966-1739, aenelson@med.unc.edu.

*The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention or the National Institutes of Health.

COMPETING INTERESTS

The authors have no competing interests to declare.

less hand rOA compared with Caucasians (4). There are also known gender differences for individual and multiple joint rOA (2, 7). Less is known about symptomatic OA (sOA), defined as the co-occurrence of joint symptoms (pain, aching, and stiffness) and rOA in a joint site. Compared with Caucasians, hip or knee sOA in African Americans tends to be of similar or higher prevalence (8, 9), and women more commonly have isolated hand, hip, or knee sOA than men (8, 10, 11), but simultaneous, multi-joint phenotypes have not been assessed. Women and African Americans may suffer greater morbidity from knee sOA (12). Due to the impact on quality of life, disability, and health care utilization, it is potentially more important to study sOA than rOA independent of clinical symptoms; given the paucity of existing data on sOA we have chosen to focus the present analysis on race and gender differences in sOA phenotypes involving the hands, knees, hips, and lumbosacral spine (LS).

PATIENTS AND METHODS

This cross-sectional analysis uses data from the Johnston County OA Project (*JoCo OA*), a prospective, longitudinal, community-based study of OA ongoing for more than 20 years. Participants were African American and Caucasian men and women aged 45 years or older, living in Johnston County, NC, who all signed informed consent (9). For the present analysis, we used a subset of data from the *JoCo OA*, collected during 2003–2010, for participants with complete symptom and radiographic data at 4 joint sites from a single visit (n=1650). The *JoCo OA* study has been continuously approved by the Institutional Review Boards of the University of North Carolina and of the Centers for Disease Control and Prevention in Atlanta, GA.

sOA was defined as the co-occurrence of both rOA and symptoms (Table 1) in the same joint site on the same side. All radiographs (supine lateral LS and anteroposterior pelvis, weight-bearing fixed-flexion posteroanterior [PA] knees, sunrise patellofemoral, and bilateral PA hands) were read for features of rOA using standard atlases by a single musculoskeletal radiologist with high reliability as previously described (4). Those participants reporting a total joint replacement at the hip or knee due to OA were included in the rOA definition; excluding these individuals did not significantly change the results. Symptoms were ascertained based on the answer to an interviewer-administered question of the format “on MOST days, do you have pain, aching, or stiffness in your [right|left] hand,” asked for 4 sites (hands, knees, hips, LS). Self-reported age, gender, and race were obtained from interviewer-administered questionnaires. Measurements of height (cm) and weight (kg), obtained during the clinic examination, were used to calculate body mass index (BMI, kg/m²).

The unit of analysis is the person. Descriptive statistics were calculated for age, BMI, race, and gender. Frequencies of sOA were determined using the definitions in Table 1. Sixteen mutually exclusive phenotypes were constructed that included all possible combinations of the 4 sOA variables. Fisher exact tests were used to compare frequencies of each phenotype (versus all others) by race and gender due to small cell sizes. A Hochberg correction (13) was applied for multiple comparisons. Logistic regression for the explanatory variables of race and gender (plus their interaction, where significant), with covariate adjustment for age and BMI, was performed for those phenotypes (as separate dependent variables) affecting at least 40 persons to allow 10 affected persons per covariate (13). Interactions between race and gender were considered noteworthy at p<0.2 and stratified analyses were performed when significant interactions were found.

RESULTS

Included participants (n=1650) were 36% men and 32% African American, with a mean age of 66 ± 10 years and mean body mass index [BMI] 31 ± 6 kg/m². Overall, the frequency of any sOA by the definitions in Table 1 was as follows: hand 13%, hip 11%, knee 25%, and LS 28%. Approximately 28% of the sample had sOA at one joint site, 15% had 2 involved joint sites, 6% had 3 involved joint sites, and 1% had sOA of all four joint sites. Fifty-one percent of the sample had no sOA at any site; otherwise the most common mutually exclusive phenotypes were LS Only (12%), Knee Only (10%), Knee/LS (5%) and Hand Only (4%). Of the 16 mutually exclusive phenotypes defined, 8 (no sOA, Hand Only, Hip Only, Knee Only, LS Only, Hand/Knee, Hand/LS, and Knee/LS) were found in more than 40 persons and included in logistic analyses.

Race differences

In unadjusted analyses (Table 2, left), African Americans compared with Caucasians were less likely to have Hand Only or Hand in some combinations; this was statistically significant for Hand Only (<1% vs. 5%) and Hand/LS (<1% vs. 3%). African Americans compared with Caucasians were more likely to have Knee Only (14% vs. 8%).

After adjustment for gender, age, and BMI (Table 3), African Americans compared with Caucasians had 80% lower odds of Hand Only (aOR 0.19, 95% CI [0.08–0.49]), 70% lower odds of the combination of Hand/Knee (aOR 0.31, 95% CI [0.13–0.76]), and 80% higher odds of Knee Only (aOR 1.78, 95% CI [1.27–2.50]).

Gender differences

In unadjusted analyses, men were more likely to have no sOA (58% vs. 46%), and were less likely than women to have Hand in some combinations (Table 2, right). This difference was statistically significant for Hand/Knee (1% vs. 3%) and Hand/Knee/LS (<1% vs. 3%). After adjustment for race, age, and BMI, compared with women, men had 50% lower odds of Hand Only and 70% lower odds of Hand/Knee (Hand Only: aOR 0.50, 95% CI [0.27–0.91]; Hand/Knee: aOR 0.31, 95% CI [0.13–0.75], Table 3), but 50% higher odds of LS Only (aOR 1.48, 95% CI [1.09–2.01]).

Due to race by gender interactions for three phenotypes, stratified analyses were performed: No sOA, Hand/LS sOA, and Knee/LS sOA (Table 3, right). Compared to Caucasian women, Caucasian men and African American men and women had approximately 50% increased odds (aOR 1.48 to 1.65) of having No sOA in any joint site. In addition, compared with Caucasian women, African American women had 93% lower odds (aOR 0.07, 95% CI [0.01–0.51]), and Caucasian men had 73% lower odds (aOR 0.27, 95% CI [0.10–0.70]) of having the combination of Hand and LS sOA, with no significant difference seen for African American men. Finally, African American women had nearly twice the odds of having the combination of Knee and LS sOA compared with Caucasian women (aOR 1.92, 95% CI [1.12–3.29]), with no significant differences for the men.

DISCUSSION

In this large community-based study of adults both with and without sOA, African Americans had lower frequencies of Hand Only or Hand in combination with other sites, and higher frequencies of Knee Only, compared with Caucasians. Men, compared with women, were less likely to have Hand Only but more likely to have LS Only. These results are similar to our previous findings using rOA alone (4), where African Americans had less frequent hand rOA (particularly of the DIPs), but more frequent tibiofemoral joint rOA and the combination of tibiofemoral and LS rOA. Men were less likely than women to have

hand rOA, and more likely than women to have the combination of tibiofemoral and LS rOA (4). These findings suggest that a definition of “generalized OA” may need to be race and gender specific.

To the best of our knowledge, there are no prior community-based studies (ie., of participants who were not originally selected for joint pain or OA) that assessed multiple joint OA phenotypes, defined by both symptom presence and radiographic findings. Relying on both clinical and radiographic data in selected populations, two studies have provided detailed estimates of sOA phenotypes. The Genetics, Arthrosis, and Progression (GARP) study, a familial study of individuals selected based on the presence of sOA, found combinations of hand/spine (cervical or lumbar), hand/knee, knee/spine, and hip/spine to be the most common (1). Cushnaghan and Dieppe assessed only limb joints (knees, hands, hips, ankles, shoulders, elbows, wrists, and feet) and found, in consecutive patients with OA referred to a rheumatology center, that only 47% had one symptomatic joint site (236/500), 36% had 2 affected sites (the majority were women with knee and hand OA), 13% had 3 affected sites, and <1% had 4+ affected sites (14). Other authors have reported similar patterns for rOA, but have not assessed symptoms (2, 3, 7). A population-based study using only ACR clinical criteria found that 72% of 230 adults with OA had a single joint affected, 15% had hand/knee, 6% had hip/knee, 4% had hand/hip/knee, and 3% had hand/hip; spine was not assessed (15).

The community-based *JoCo OA* provides a unique opportunity to assess multiple joint sOA phenotypes in a way that may be generalizable to the community as opposed to a clinic-based population. We found that LS Only, Knee Only, and LS/Knee were the most common phenotypes, with significant differences by race and gender; these demographic characteristics should be taken into account when defining multiple joint, or “generalized” OA involvement.

Acknowledgments

We would like to thank our funding sources and the staff and participants of the Johnston County Osteoarthritis Project, without whom this work would not be possible.

Funding for this project was provided in part by: ACR-REF Clinical Investigator Fellowship Award 2009 (Nelson); NIAMS K23-AR061406 (Nelson); Arthritis Foundation Postdoctoral Fellowship Award (Golightly); CDC/ Association of Schools of Public Health S043 and S3486 (Jordan, Renner); NIAMS P60-AR30701 (Jordan, Renner, Schwartz); NIH/NIA Claude D. Pepper 5-P30-AG028716 and Grant P01 AR050245 from NIAMS (Kraus).

REFERENCE LIST

1. Riyazi N, Meulenbelt I, Kroon HM, Roday KH, Hellio le Graverand MP, Rosendaal FR, et al. Evidence for familial aggregation of hand, hip, and spine but not knee osteoarthritis in siblings with multiple joint involvement: the GARP study. *Ann Rheum Dis*. 2005; 64(3):438–43. [PubMed: 15458958]
2. Cvijetic S, Campbell L, Cooper C, Kirwan J, Potocki K. Radiographic osteoarthritis in the elderly population of Zagreb: distribution, correlates, and the pattern of joint involvement. *Croat Med J*. 2000; 41(1):58–63. [PubMed: 10810169]
3. Kraus VB, Jordan JM, Doherty M, Wilson AG, Moskowitz R, Hochberg M, et al. The Genetics of Generalized Osteoarthritis (GOGO) study: study design and evaluation of osteoarthritis phenotypes. *Osteoarthritis Cartilage*. 2007; 15(2):120–7. [PubMed: 17113325]
4. Nelson AE, Renner JB, Schwartz TA, Kraus VB, Helmick CG, Jordan JM. Differences in multijoint radiographic osteoarthritis phenotypes among African Americans and Caucasians: The Johnston County Osteoarthritis project. *Arthritis Rheum*. 2011; 63(12):3843–52. [PubMed: 22020742]
5. Nelson AE, Braga L, Renner JB, Atashili J, Woodard J, Hochberg MC, et al. Characterization of individual radiographic features of hip osteoarthritis in African American and White women and

- men: the Johnston County Osteoarthritis Project. *Arthritis Care Res (Hoboken)*. 2010; 62(2):190–7. [PubMed: 20191517]
6. Braga L, Renner JB, Schwartz TA, Woodard J, Helmick CG, Hochberg MC, et al. Differences in radiographic features of knee osteoarthritis in African-Americans and Caucasians: the Johnston county osteoarthritis project. *Osteoarthritis Cartilage*. 2009; 17(12):1554–61. [PubMed: 19735758]
 7. Hirsch R, Lethbridge-Cejku M, Scott WW Jr, Reichle R, Plato CC, Tobin J, et al. Association of hand and knee osteoarthritis: evidence for a polyarticular disease subset. *Ann Rheum Dis*. 1996; 55(1):25–9. [PubMed: 8572729]
 8. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of hip symptoms and radiographic and symptomatic hip osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol*. 2009; 36(4):809–15. [PubMed: 19286855]
 9. Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol*. 2007; 34(1):172–80. [PubMed: 17216685]
 10. Oliveria SA, Felson DT, Reed JI, Cirillo PA, Walker AM. Incidence of symptomatic hand, hip, and knee osteoarthritis among patients in a health maintenance organization. *Arthritis Rheum*. 1995; 38(8):1134–41. [PubMed: 7639811]
 11. Niu J, Zhang Y, LaValley M, Chaisson CE, Aliabadi P, Felson DT. Symmetry and clustering of symptomatic hand osteoarthritis in elderly men and women: the Framingham Study. *Rheumatology (Oxford)*. 2003; 42(2):343–8. [PubMed: 12595633]
 12. Losina E, Walensky RP, Reichmann WM, Holt HL, Gerlovin H, Solomon DH, et al. Impact of obesity and knee osteoarthritis on morbidity and mortality in older Americans. *Ann Intern Med*. 2011; 154(4):217–26. [PubMed: 21320937]
 13. Hochberg Y. A Sharper Bonferroni Procedure for Multiple Tests of Significance. *Biometrika*. 1988; 75(4):800–2.
 14. Cushnaghan J, Cooper C, Dieppe P, Kirwan J, McAlindon T, McCrae F. Clinical assessment of osteoarthritis of the knee. *Ann Rheum Dis*. 1990; 49(10):768–70. [PubMed: 2241265]
 15. Mannoni A, Briganti MP, Di Bari M, Ferrucci L, Costanzo S, Serni U, et al. Epidemiological profile of symptomatic osteoarthritis in older adults: a population based study in Dicomano, Italy. *Ann Rheum Dis*. 2003; 62(6):576–8. [PubMed: 12759299]

TABLE 1

Definitions of Symptomatic OA *

Joint Site	Symptoms [†]	AND	Radiographic OA criteria
Hand	hand	+	KL 2 in at least one DIP AND at least 3 total hand joints
Knee	knee	+	Tibiofemoral joint KL 2 OR patellofemoral osteophyte 2 [‡] OR TJR [§]
Hip	hip	+	Hip joint KL 2 OR TJR [§]
LS	low back	+	Disc narrowing AND an osteophyte 1 at the same level (L1/2-L5/S1) [‡]

* Symptomatic OA requires both symptoms and radiographic criteria in the same joint site, on the same side

[†] Answered yes to: “on MOST days do you have pain, aching, or stiffness of your ____?”

[‡] Osteophyte and disc narrowing graded 0–3 according to the Burnett atlas

[§] Joint replacement at knee or hip done for OA per participant report

KL=Kellgren Lawrence grade, DIP=Distal Interphalangeal joint, LS=Lumbosacral Spine, TJR=Total Joint Replacement

TABLE 2
 Unadjusted frequencies of multiple joint symptomatic osteoarthritis phenotype by race and gender (n=1650).

Symptomatic OA Phenotype*	Overall n (%)	Comparisons by Race			Comparisons by Gender		
		Caucasian n (%)	African American n (%)	Fisher exact p value†	Women n (%)	Men n (%)	Fisher exact p value†
No OA	836 (50.7)	544 (48.6)	292 (55.1)	0.015	488 (46.4)	348 (58.1)	< 0.001
Hand Only	64 (3.9)	59 (5.3)	5 (0.9)	< 0.001	50 (4.8)	14 (2.3)	0.016
Hip Only	45 (2.7)	33 (3.0)	12 (2.3)	0.518	25 (2.4)	20 (3.3)	0.272
Knee Only	162 (9.8)	87 (7.8)	75 (14.2)	< 0.001	115 (10.9)	47 (7.9)	0.048
LS Only	195 (11.8)	136 (12.1)	59 (11.1)	0.569	108 (10.3)	87 (14.5)	0.011
Hand/Hip	13 (0.8)	12 (1.1)	1 (0.2)	0.073	11 (1.1)	2 (0.3)	0.151
Hand/Knee	42 (2.6)	36 (3.2)	6 (1.1)	0.011	36 (3.4)	6 (1.0)	0.002
Hand/LS	42 (2.6)	38 (3.4)	4 (0.8)	0.001	34 (3.2)	8 (1.3)	0.022
Hip/Knee	26 (1.6)	20 (1.8)	6 (1.1)	0.400	12 (1.1)	14 (2.3)	0.067
Hip/LS	28 (1.7)	20 (1.8)	8 (1.5)	0.839	21 (2.0)	7 (1.2)	0.239
Knee/LS	88 (5.3)	50 (4.5)	38 (7.2)	0.026	60 (5.7)	28 (4.7)	0.425
Hand/Hip/Knee	6 (0.4)	6 (0.5)	0 (0)	0.186	5 (0.5)	1 (0.2)	0.426
Hand/Hip/LS	17 (1.0)	15 (1.3)	2 (0.4)	0.113	16 (1.5)	1 (0.2)	0.009
Hand/Knee/LS	32 (1.9)	28 (2.5)	4 (0.8)	0.020	30 (2.9)	2 (0.3)	< 0.001
Hip/Knee/LS	37 (2.2)	25 (2.2)	12 (2.3)	1.000	24 (2.3)	13 (2.2)	1.000
All sites	17 (1.0)	11 (1.0)	6 (1.0)	0.797	16 (1.5)	1 (0.2)	0.009
Total	1650 (100)	1120 (100)	530 (100)	--	1051 (100)	599 (100)	--

* Mutually exclusive, referent is all other phenotypes

† After Hochberg adjustment for multiple comparisons, BOLD indicates statistically significant differences

LS=lumbosacral spine

TABLE 3

Adjusted* Odds Ratios (and 95% Confidence Intervals) for Frequencies of Symptomatic OA Phenotypes by Race and by Gender ($n=1650$).

Symptomatic OA Phenotype [†]	<i>n</i>	aOR (95% CI) for AA vs White	aOR (95% CI) for Men vs Women	Race and Gender stratified [‡]
No sOA	836	--	--	White women: 1.0 (referent)
				White men: 1.65 (1.28, 2.13)
				AA women: 1.57 (1.19, 2.07)
				AA men: 1.48 (1.05, 2.09)
				--
Hand Only	64	0.19 (0.08, 0.49)	0.50 (0.27, 0.91)	--
Hip Only	45	0.77 (0.39, 1.51)	1.38 (0.75, 2.51)	--
Knee Only	162	1.78 (1.27, 2.50)	0.85 (0.59, 1.22)	--
LS Only	195	0.90 (0.65, 1.25)	1.48 (1.09, 2.01)	--
Hand/Knee	42	0.31 (0.13, 0.76)	0.31 (0.13, 0.75)	--
Hand/LS	42	--	--	White women: 1.0 (referent)
				White men: 0.27 (0.10, 0.70)
				AA women: 0.07 (0.01, 0.51)
Knee/LS	88	--	--	AA men: 0.41 (0.12, 1.37)
				White women: 1.0 (referent)
				White men: 1.23 (0.69, 2.20)
				AA women: 1.92 (1.12, 3.29)
				AA men: 1.18 (0.52, 2.64)

* Adjusted for race, gender, age, and body mass index, only for those phenotypes affecting at least 40 persons

[†] Mutually exclusive, referent is all other phenotypes

[‡] Stratified by race and gender due to a significant (<0.2) race*gender interaction term: for no sOA $p=0.02$, for Hand/LS $p=0.02$, and for knee/LS $p=0.17$

BOLD indicates statistically significant results (aOR does not cross 1.0)

aOR=adjusted odds ratio, CI=confidence interval, AA=African American, LS=Lumbosacral Spine