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Frailty and Hip Osteoarthritis in Men in the MrOS Cohort

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Background. Frailty has been associated in previous studies with increased mortality and morbidity, but little has been published on its association with arthritis. This study examined the association of hip osteoarthritis to frailty status in a longitudinal observational cohort of older men in the Osteoporotic Fractures in Men Study.

Methods. Participants ($N = 4,130$) were men aged 65 years and older with complete frailty status and hip radiographs. We defined frailty as three or more of the following components: unintentional weight loss, weakness, self-reported exhaustion, low activity level, and slow walking speed. Men with intermediate stage status met one or two criteria while robust men had none. We defined radiographic hip osteoarthritis (RHOA) as a modified Croft score greater than or equal to 2 on hip radiograph. The relation of RHOA or total hip replacement (THR) to frailty status was examined in cross-sectional and incident analyses using logistic regression.

Results. Prevalence of robust, intermediate, and frail status was 50%, 42%, and 8%, respectively. RHOA or THR was associated with increased odds of being frail or intermediate compared with robust (adjusted odds ratio = 1.45, 95% confidence interval [CI] 1.18, 1.78). Men with RHOA or THR were 1.27 times more likely to have incident frail or intermediate status compared with robust (95% CI: 1.19, 1.38).

Conclusions. RHOA and THR are associated with greater frailty status in older men, suggesting that interventions to reduce frailty should be evaluated in older men with either RHOA or THR.

Key Words: Osteoarthritis—Hip—Frailty—Older men.

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OSTEOARTHRITIS (OA) is the most common form of arthritis and the most common cause of disability in the elderly adult. Frailty has been associated in previous studies with increased mortality and morbidity related to falls, cardiovascular disease, hospitalization, and disability (1). Also, frailty has been found to be associated with a variety of other comorbidities in the past (2–4). However, the association of hip OA to frailty has not been thoroughly evaluated.

Frailty as defined by Fried and colleagues (5) using data collected in the Cardiovascular Health Study required the presence of at least three of five components, including unintentional weight loss, slow walking speed, low grip strength, low level of physical activity, and reduced energy level. A frailty index similar to that developed in the Cardiovascular Health Study predicted risk of incident disability, falls, fracture, and mortality in the Osteoporotic Fractures in Men (MrOS) cohort, a longitudinal study of older men examining risk factors for osteoporosis and aging (6,7).

OA is a disease associated with older age and with prior injury to joints (8). It also has associations with other comorbidities, in particular with obesity (9–11). One of the primary functional limitations associated with OA is mobility limitation, in particular lower limb mobility. Given these features, which parallel or augment frailty manifestations, we evaluated the association of frailty with hip OA. Most total hip replacements (THR) are performed as treatments for hip OA, and undergoing such a procedure in the absence of hip fracture is often included as a proxy for advanced hip OA. In this study, we explored whether hip OA or hip OA inclusive of THR are associated with cross-sectional frailty or with incident worsening frailty in older community-dwelling men participating in the MrOS study.

Methods

Participants

The MrOS study consists of 5,994 community-dwelling men aged 65 years and older recruited from six U.S. clinical centers (Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; the Monongahela Valley near

Pittsburgh, Pennsylvania; Portland, Oregon; and San Diego, California) for a baseline visit between March 2000 and April 2002. Participants were required to be ambulatory and not have had bilateral hip replacements. The institutional review board at each participating institution approved the study protocol, and written informed consent was obtained from all participants. Participants returned for a second clinic visit (Visit 2) between March 2005 and May 2006 and a third clinic visit (Visit 3) between March 2007 and March 2009. A description of the MrOS cohort has been published (12,13).

Covariate Data

All covariates were assessed at the second clinic visit. Height (centimeters) was measured on Harpenden stadiometers and weight (kilograms) by standard balance beam or digital scales using standard protocols. Body mass index (BMI) was calculated as kg/m^2. Appendicular skeletal mass and total and percent body fat were determined from whole-body dual-energy x-ray absorptiometry on Hologic (Bedford, MA) QDR4500W scanners using standardized protocols. Questionnaires ascertained information on ethnicity, self-rated health (excellent/good vs fair/poor/very poor), education (college education vs less), and medical history (cancer, stroke, diabetes, low or high thyroid, Parkinson's disease, heart attack, congestive heart failure, chronic obstructive pulmonary disease, and hypertension). Comorbidity was assessed as the sum of the above-mentioned conditions. Hip pain was ascertained using the question "In the PAST 30 DAYS, have you experienced pain in your RIGHT HIP?" (The same question was then asked for the left hip.) The Physical Activity Scale for the Elderly (14), with higher score representing greater activity, was used to measure physical activity. Participants completed the Medical Outcomes Study 12-item Short Form (15) for assessment of quality of life. Functional limitation was defined as self-reported inability to walk 2–3 blocks or climb 10 steps without resting, and instrumental activities in daily living limitation was defined as self-reported inability to prepare meals, complete heavy housework, or shop.

Measurement of Radiographic OA

Hip radiographs were obtained at Visit 2 with the subject standing, using a standardized footmat with toes internally rotated 15°, and the x-ray beam positioned two inches above the pubis symphysis (16). The following five individual radiographic features of OA: (1) joint space narrowing (0–4) laterally and medially; (2) osteophyte formation (0–3; femoral or acetabular and either inferiorly or superiorly in each location); (3) cysts (0–3); (4) subchondral sclerosis (0–3); and (5) femoral head deformity (0–3) (17) were measured using the radiographs. Atlas figures were consulted during the readings to improve reliability (18).

Each hip was assigned a summary grade for radiographic hip osteoarthritis (RHOA) severity of 0–4, using the modified Croft score. Croft Grade 2 hips had the presence of definite (severity grade ≥2) joint space narrowing or osteophytes, and Grades 3 and 4 required additional other features (cysts or subchondral sclerosis, deformity). Participants with a hip summary grade of greater than or equal to 2 were classified as having RHOA. In addition, each hip was reviewed for a THR. All self-reported THRs at Visit 2 were verified using the radiograph by a qualified radiologist, and a validated THR variable was created. All hip fractures from baseline to Visit 2 were excluded from the analysis to ensure that THR was not a result of a hip fracture. We also excluded men with Paget's disease in either hip joint.

All radiographs were centrally assessed by the primary reader who was blinded to participants' clinical characteristics. A random sample of radiographs ($N = 472$ films) were re-read by the primary reader for reliability. The intrareliability scores were as follows: the kappa for the maximum definite joint space narrowing and definite osteophyte score was 0.81, the kappa was 0.71 for femoral osteophytes, and for lateral or medial joint space narrowing and osteophytes the kappa was 0.81 (19).

We based the analyses on the hip with highest (worst) Croft score (RHOA summary score) of the two hips within an individual participant.

We analyzed OA using the following three different definitions:

1. *RHOA* or *THR* (primary definition): Croft greater than or equal to 2 in the worst hip or the presence of a THR, compared with Croft less than or equal to 1 in the worst hip and no THR, regardless of reported hip pain
2. *RHOA irrespective of THR* (secondary definition): Croft greater than or equal to 2 in the worst hip, compared with Croft less than or equal to 1 in the worst hip (regardless of the presence of THR and/or hip pain)
3. *Clinical OA* (tertiary definition): We defined four categories of clinical OA as follows:

   - Symptomatic clinical OA: defined as men with hip pain and either RHOA (Croft ≥2) or THR;
   - Hip pain only: defined as men with hip pain but no RHOA or THR;
   - Asymptomatic clinical OA: defined as no hip pain but with either RHOA or THR;
   - No clinical OA: defined as no hip pain and no RHOA or THR.

Frailty

The frailty definition used in this study was derived from a modified version of the definition used in the Cardiovascular Health Study (5) and has been used in previous analyses in MrOS (7). The modified Cardiovascular Health Study definition uses five components to define the

presence of frailty: weight loss greater than 5% between baseline and Visit 2 (by direct measurement of body weight), weakness (weakest 20% of grip strength, stratified by BMI), slowness (slowest 20% in walking speed over a 6-m course, stratified by height), low activity level (lowest 20% of Physical Activity Scale for the Elderly score [range 0–486]), and exhaustion (self-report from question on 12-item short form: "How much of the time during the past four weeks did you have a lot of energy?" [a little/none of the time = exhaustion]). Frail is defined as having three or more of these components, intermediate stage defined as having from one to two components, and participants having none of the components are defined as being robust. Frailty was defined at the second MrOS clinic visit, with weight loss calculated from baseline to Visit 2. Similarly, frailty defined at the third clinic visit calculated weight loss from Visit 2 to Visit 3.

Participants in Cross-sectional Analysis

Men who had RHOA measurements and frailty data for greater than or equal to 3 of the frailty components were included in the cross-sectional analyses ($N = 4,130$).

Participants Included in the Longitudinal Analyses

Longitudinal analysis was conducted in 3,237 men who were either robust or intermediate stage at Visit 2, returned for the third clinic visit and had no missing data for frailty status. Among these men, at Visit 3, 1,599 (49%) were robust, 1,392 (43%) were intermediate stage, and 246 (8%) were frail. Average follow-up time between the visits was 2.3 ± 0.36 years.

Statistical Analysis

To account for known and potential confounding, covariates were compared among participants with RHOA or THR to those without either RHOA or THR. We also compared participant characteristics across categories of frailty status using analysis of variance for normally distributed continuous variables, non-parametric Wilcoxon tests for skewed continuous variables, and chi-square tests for categorical variables. Covariates that were significantly associated with both RHOA or THR and frailty were included in the models, but we excluded covariates that were used to define the frailty syndrome (such as physical activity or percent body fat) and those that we believed to be the result of frailty, such as limitation of instrumental activities of daily living and self-rated health on the models. Multivariate models were adjusted for age, clinic site, BMI, college education, and number of comorbid medical conditions.

In cross-sectional and longitudinal models, and to account for the three level structure of frailty, we dichotomized the frailty outcome into two categories: frail (vs intermediate stage or robust) and frail or intermediate stage (vs robust) and ran a logistic regression model for each outcome.

Statistical analyses were completed using SAS version 9.2 (SAS Inc., Cary, NC) and Stata version 10 (Stata Corp., College Station, TX).

Results

We evaluated 4,130 men with a mean age of 71.3 (±5.4) years and mean BMI of 27.4 (±4.0) kg/m^2. Of these, 512 had RHOA or THR. A total of 137 had validated THR, of whom 41 had RHOA in one hip and THR in the contralateral hip and 96 had THRs with no OA in contralateral hip. Prevalence of robust, intermediate, and frailty status was 50%, 42%, and 8% at Visit 2, respectively.

Greater or worsening frailty status was associated with higher age, shorter height, less weight (but not with BMI), and with increasing numbers of medical conditions and with poorer self-rated health (Table 1). Ethnic/racial characteristics were similar across the three frailty groups, but worse frailty status was associated with lower education level (Table 1).

Cross-sectional Analysis for RHOA or THR

In the cross-sectional analyses, men with our primary definition of RHOA or THR were more likely to have worse frailty status than those with neither RHOA nor THR. In multivariate models, men with RHOA or THR were 1.44 times more likely to be classified as frail (95% confidence interval [CI]: 1.06–1.96) compared with intermediate/robust, and 1.45 times more likely to be frail/intermediate (95% CI: 1.18–1.78) compared with robust. In our secondary analyses, the association between men with RHOA irrespective of THR and frailty was somewhat less strong. In multivariate models, men with RHOA irrespective of THR were not significantly more likely to be classified as frail compared with intermediate/robust (odds ratio [OR]: 1.23, 95% CI: 0.87–1.74), but were more likely to be classified as frail/intermediate versus robust (multivariable-adjusted OR = 1.32, 95% CI 1.05–1.65).

Cross-sectional Analysis of Clinical OA

In our tertiary analyses, compared with men without clinical OA, those with symptomatic, asymptomatic, or hip pain only were more likely to be classified with worse frailty status. Men with symptomatic OA were more likely to be frail or intermediate stage (vs robust) than those with no clinical OA (multivariable-adjusted OR = 1.57, 95% CI 1.1–2.22). Men with asymptomatic OA were more likely to be frail (vs intermediate stage or robust) compared with men with no clinical OA (OR = 1.54, 95% CI 1.0–2.38). The magnitude of this association was reduced and became nonsignificant in frail or intermediate stage men (vs robust; multivariable-adjusted OR = 1.29, 95% CI 0.97–1.71). A similar association

Table 1. Characteristics of Men at Visit 2 According to Their Frailty Category

Visit 2 Characteristics	Robust (N = 2,070)	Intermediate Stage (N = 1,724)	Frail (N = 336)	p-Value
Age	75.62 ± 4.5	78.49 ± 5.45	81.81 ± 5.71	<.001
Body mass index (kg/m^2)	27.38 ± 3.51	27.34 ± 4.27	27.47 ± 4.83	0.103
Height (m)	174.35 ± 6.66	172.76 ± 6.89	170.94 ± 6.91	<.001
Weight (kg)	83.31 ± 12.25	81.74 ± 14.52	80.37 ± 15.64	<.001
Race/ethnicity				0.087
White	1,876 (90.6)	1,549 (89.9)	310 (92.3)	
African American	55 (2.7)	66 (3.8)	11 (3.3)	
Asian	66 (3.2)	61 (3.5)	10 (3.0)	
Hispanic	49 (2.4)	23 (1.3)	3 (0.9)	
Other	24 (1.2)	25 (1.5)	2 (0.6)	
Self-rated health	1,958 (94.6)	1,436 (83.3)	184 (54.8)	<.001
College education	1,242 (60)	907 (52.6)	139 (41.4)	<.001
Instrumental activities of daily living limitation	110 (5.3)	305 (17.8)	185 (56.6)	<.001
Walking speed	1.24 ± 0.17	1.07 ± 0.22	0.81 ± 0.21	<.001
Grip strength (kg)	43.63 ± 6.77	37.28 ± 8.24	30.18 ± 6.82	<.001
Physical Activity Scale for the Elderly score	164.86 ± 59.41	117.32 ± 64.15	58.91 ± 42.04	<.001
Number of medical conditions	1.21 ± 1.04	1.52 ± 1.19	2.13 ± 1.41	<.001
Hip pain on either side	515 (24.9)	495 (28.7)	130 (38.7)	<.001
Croft Grade (0–4)				<.001
0	1,354 (65.4)	1,043 (60.5)	189 (56.3)	
1	551 (26.6)	482 (28.0)	95 (28.3)	
2	93 (4.5)	114 (6.6)	33 (9.8)	
3	54 (2.6)	59 (3.4)	13 (3.9)	
4	17 (0.8)	26 (1.5)	6 (1.8)	
Croft ≥2 in worst hip	164 (7.9)	199 (11.5)	52 (15.5)	<.001
Validated total hip replacement	48 (2.3)	69 (4)	21 (6.3)	0.001

was detected in men with hip pain only compared with those with no clinical OA, where men with hip pain only were more likely to be frail (vs intermediate stage or robust; multivariable-adjusted OR = 1.68, 95% CI 1.28–2.2) and where men with hip pain only were also more likely to be frail or intermediate stage (vs robust; multivariable-adjusted OR = 1.22, 95% CI 1.04–1.43; Table 2).

Longitudinal Analysis of RHOA or THR

Longitudinal associations with frailty categories were similar to the cross-sectional associations for RHOA or THR and for RHOA irrespective of THR in multivariable adjusted models: RHOA or THR and RHOA irrespective of THR at Visit 2 were significantly associated with worsening of frailty status from Visit 2 to Visit 3 among 3,237 participants who were robust or intermediate stage at Visit 2. Men with RHOA or THR were 1.27 times more likely to be classified as frail or intermediate stage (95% CI: 1.19, 1.38) compared with robust, and 1.26 times more likely to be frail (95% CI: 1.14, 1.37) compared with intermediate or robust. In our secondary analyses, the association between men with RHOA irrespective of THR and frailty was very similar (see Table 3).

Longitudinal Analysis of Clinical OA

Clinical OA was strongly associated with worsening frailty. Men with symptomatic OA at Visit 2 were more likely to be frail at Visit 3 (vs intermediate stage or robust) than were men with no clinical OA (OR = 1.65, 95% 1.0–2.71) after adjustment of covariates. The strength of the association became markedly smaller and less significant when examining frail or intermediate stage men (vs robust) with symptomatic clinical OA compared with men with no clinical OA. Hip pain only or asymptomatic clinical OA compared with no hip pain was moderately associated with the frailty categories in the longitudinal analysis (Table 3).

Discussion

Frailty is an important measure of overall health status and has in past studies been found to be associated with outcomes including death. Hip OA is a common and disabling condition, with available treatments ranging from relatively simple (medication) to complex (joint replacement). Identifying an association between the two is valuable in that it may serve to focus the attention of clinicians on hip OA as a modifiable component of health status if there are known implications with regard to frailty.

There is a moderate to strong cross-sectional association of RHOA and THR with frailty in older men. We also found evidence of a longitudinal association between RHOA or RHOA and THR and subsequent increasing frailty status.

In our analysis, including THR with RHOA essentially did not change or in some cases strengthened the apparent

Table 2. Multivariate Adjusted Odds Ratios and 95% Confidence Interval for Cross-sectional Association of Radiographic Hip Osteoarthritis With Frailty Status

OA Definition	*N*	Model	Frail vs Intermediate Stage or Robust (*N* = 336)	Frail/Intermediate Stage vs Robust (*N* = 2,060)
Croft ≥2 or THR	512	Age adjusted	1.56 (1.16–2.1)	1.5 (1.23–1.83)
		MV adjusted*	1.44 (1.06–1.96)	1.45 (1.18–1.78)
Croft <2 and no THR	3,619		1.00 (referent)	1.00 (referent)
Croft ≥2	415	Age adjusted	1.38 (0.99–1.92)	1.37 (1.1–1.71)
		MV adjusted*	1.23 (0.87–1.74)	1.32 (1.05–1.65)
Croft <2	3,715		1.00 (referent)	1.00 (referent)
Clinical OA				
Age adjusted				
Symptomatic OA	219		1.6 (0.95–2.7)	1.64 (1.17–2.31)
Asymptomatic	293		1.78 (1.17–2.69)	1.37 (1.04–1.81)
Hip pain only	921		1.95 (1.5–2.53)	1.31 (1.12–1.53)
No clinical OA	2,697		1.00 (referent)	1.00 (referent)
MV adjusted				
Symptomatic OA	219		1.34 (0.77–2.31)	1.57 (1.1–2.22)
Asymptomatic	293		1.54 (1–2.38)	1.29 (0.97–1.71)
Hip pain only	921		1.68 (1.28–2.2)	1.22 (1.04–1.43)
No clinical OA	2,697		1.00 (referent)	1.00 (referent)

Notes: MV = multivariable; OA = osteoarthritis; THR = total hip replacement.
*MV models adjusted for age, clinic site, body mass index, college education, and number of comorbidities.

Table 3. Incident Odds Ratios for Association of Radiographic Hip Osteoarthritis With Worsening of Frailty Status From Visit 2 to Visit 3 Among Those Robust or Intermediate Stage at Visit 2 (*N* = 3,237)

OA Definition	*N* at Visit 3	Model	Frail vs Intermediate Stage/Robust *N* = 246	Frail/Intermediate Stage vs Robust *N* = 1,638
Croft ≥2 or THR	378	Age adjusted	1.17 (1.14–1.2)	1.12 (1.11–1.14)
		MV adjusted*	1.26 (1.14–1.37)	1.27 (1.19–1.38)
Croft <2 and no THR	2,859		1.00 (referent)	1.00 (referent)
Croft ≥2	309	Age adjusted	1.17 (1.14–1.2)	1.13 (1.11–1.14)
		MV adjusted*	1.22 (1.08–1.37)	1.24 (1.16–1.33)
Croft <2	2,927		1.00 (referent)	1.00 (referent)
Clinical OA				
Age adjusted				
Symptomatic OA	159		1.73 (1.06–2.8)	1.19 (0.87–1.62)
Asymptomatic	219		1.33 (0.97–1.83)	1.32 (1.11–1.57)
Hip pain only	702		1.17 (1.14–1.2)	1.13 (1.11–1.14)
No clinical OA	2,156		1.00 (referent)	1.00 (referent)
MV adjusted				
Symptomatic OA	159		1.65 (1–2.71)	1.09 (0.79–1.49)
Asymptomatic	219		1.2 (0.87–1.66)	1.25 (1.04–1.49)
Hip pain only	702		1.19 (1.16–1.23)	1.13 (1.12–1.15)
No clinical OA	2,156		1.00 (referent)	1.00 (referent)

Notes: MV = multivariable; OA = osteoarthritis; THR = total hip replacement.
*MV models adjusted for age, clinic site, body mass index, college education, and number of comorbidities.

association with frailty. This observation may not be surprising and likely derives from an underlying association between RHOA and frailty (we excluded all THRs performed for the diagnosis of hip fracture, so the THRs in this analysis represent only OA-related surgeries). One possibility is that men did not derive benefit from the THR procedure at a level that allowed for modification of their frailty status. However, the potential benefit of THR with regard to improvement of frailty status could only be definitively established in the context of a randomized clinical trial, which is unlikely to be performed in the near future. As our results stand now, the clinical implication is that men with THR should be considered to be at increased risk of frailty similar to those with hip OA who have not undergone surgical treatment.

There is approximately a 25%–75% increased likelihood of being frail or intermediate stage if one has hip OA, depending on the definition of hip OA used. Consistency across a variety of OA definitions suggests that the findings are relatively robust and apply to clinically important manifestations of OA.

This may be because hip OA exerts its effect through a variety of mechanisms. White and colleagues (20) have recently reported that older adults with a fast decline in gait speed have a 90% greater risk of mortality than those with slow decline; it is possible that a component of decline in gait speed may be due to hip OA. Given that there is no single manifestation of hip OA (eg, pain or radiographic disease) that is primarily associated with frailty, the most important clinical message should be that physicians caring for men with hip OA should be cognizant of the potential for co-extant frailty.

There were limitations to our study. First, the number of THRs was small in this group limiting our power to detect any association. Second, the study population only included older men, and the results may not generalize to women. Third, the follow-up time from Visit 2 to Visit 3 was 2.3 years, which may not be enough time for improvement after THR to be evident, and we did not have information about the timing of THR so could not perform analyses related to time between surgery and frailty outcome. Our analytic group is comparable in terms of prevalence of frailty (8%) and intermediate stage (42%) to prevalence figures reported for other groups of community-dwelling persons aged 65 years and older (21). Despite this, the fact that we have used a distributional approach to define frailty may limit the generalizability of our findings to other studies. Finally, residual confounding and causal effects of THR on frailty cannot be established in an observational setting.

There were also significant strengths to our study. First, the overall cohort was large, and loss to follow up was relatively small over a number of years. The study variables were well characterized and collected carefully at every point. The radiographs were read by expert readers and these reads have been evaluated for reliability and used in other studies successfully.

In conclusion, RHOA and THR are associated with frailty in older men, and interventions to reduce frailty should be evaluated in this population with either RHOA or THR.

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Conflict of Interest

None.

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