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Obesity and sex influence fatty infiltration of the rotator cuff: the Rotator Cuff Outcomes Workgroup (ROW) and Multicenter Orthopaedic Outcomes Network (MOON) cohorts

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Background: Fatty infiltration (FI) is one of the most important prognostic factors for outcomes after rotator cuff surgery. Established risk factors include advancing age, larger tear size, and increased tear chronicity. A growing body of evidence suggests that sex and obesity are associated with FI; however, data are limited.
Methods: We recruited 2 well-characterized multicenter cohorts of patients with rotator cuff tears (Multicenter Orthopaedic Outcomes Network [MOON] cohort [n = 80] and Rotator Cuff Outcomes Workgroup [ROW] cohort [n = 158]). We used multivariable logistic regression to evaluate the relationship between body mass index (BMI) and the presence of FI while adjusting for the participant's age at magnetic resonance imaging, sex, and duration of shoulder symptoms, as well as the cross-sectional area of the tear. We analyzed the 2 cohorts separately and performed a meta-analysis to combine estimates.
Results: A total of 27 patients (33.8%) in the Multicenter Orthopaedic Outcomes Network (MOON) cohort and 57 patients (36.1%) in the Rotator Cuff Outcomes Workgroup (ROW) cohort had FI. When BMI < 25 kg/m^2 was used as the reference category, being overweight was associated with a 2.37-fold (95% confidence interval [CI], 0.77-7.29) increased odds of FI and being obese was associated with a 3.28-fold (95% CI, 1.16-9.25) increased odds of FI. Women were 4.9 times (95% CI, 2.06-11.69) as likely to have FI as men.
Conclusions: Among patients with rotator cuff tears, obese patients had a substantially higher likelihood of FI. Further research is needed to assess whether modifying BMI can alter FI in patients with rotator cuff tears. This may have significant clinical implications for presurgical surgical management of rotator cuff tears. Sex was also significantly associated with FI, with women having higher odds of FI than men. Higher odds of FI in female patients may also explain previously reported early suboptimal outcomes of rotator cuff surgery and higher pain levels in female patients as compared with male patients.
Level of evidence: Level II; Retrospective Multivariable Design; Prognosis Study

Keywords: Rotator cuff; fatty infiltration; obesity; body mass index; sex; cross-sectional study

Shoulder pain was the cause of an estimated 9.6 million annual patient visits, on average, in ambulatory settings in the United States in 2015-2016.[39] This resulted in an average estimated rate of 3.9 visits per 100 US adults. Rotator cuff tears are presumed to be the leading cause of shoulder pain and disability, leading to an estimated arthroscopic rotator cuff surgery rate of 11.94-185.35 per 100,000 persons across US states.[23] Fatty infiltration (FI) of the rotator cuff muscles is critical for surgical decision making because higher grades of FI are associated with worse outcomes.[13,14,26,31,32,36,42,43,45] However, FI does not develop in all patients with rotator cuff tears. In addition to established characteristics such as increasing age, larger tear size, and increased tear chronicity,[16,34,35] there is limited evidence that obesity is associated with FI.[8,28,33] The association of obesity with FI needs to be further assessed in larger studies and will inform modifiable factors that are associated with the development of FI in patients with rotator cuff tears. Men and women, on average, differ in body fat composition throughout their lifetimes and also have differential distributions of fat,[12,17,25,44] and data are limited on whether fat distribution in the rotator cuff also differs by sex.

We performed cross-sectional investigations of 2 well-characterized cohorts of patients with rotator cuff tears. The primary goal of this study was to evaluate the relationship between body mass index (BMI) and FI in men and women with rotator cuff tears.

Methods

Patient populations

Rotator Cuff Outcomes Workgroup cohort

The Rotator Cuff Outcomes Workgroup (ROW) cohort was recruited from 3 academic centers and 1 community center between February 2011 and June 2015. Patients aged 45 years or older who had symptomatic rotator cuff tears were followed up. Additional details of this cohort have been previously published.[7,18-22] There were a total of 158 patients from the ROW cohort with rotator cuff tears confirmed by magnetic resonance imaging (MRI) who had images to permit assessment of FI and were included in our analysis.

Multicenter Orthopaedic Outcomes Network cohort

The Multicenter Orthopaedic Outcomes Network (MOON) cohort is a well-defined cohort of patients with rotator cuff tears who were recruited from 10 sites across the United States. The cohort was recruited from January 2007 to January 2011, and patients aged 18 years or older were included. Additional details of this cohort have been previously published.[9,10,15,27] Patients from the MOON cohort with rotator cuff tears confirmed by MRI who had images of sufficient quality to permit assessment of FI (n = 80) and information available on BMI were included in our analysis.

Structured assessments

Patients in both cohorts filled out a baseline questionnaire on which duration of symptoms was self-reported. BMI was calculated from a patient's height and weight primarily based on self-report from structured questionnaires administered at the time of study recruitment. If height or weight was missing, this information was abstracted from the patient's electronic medical record using measures from visits prior to and inclusive of the recruitment visit.

FI and tear size of rotator cuff

Shoulder experts (fellowship-trained attending physicians) read the shoulder MRI scans for the ROW cohort. The methodology of MRI review for the ROW cohort has been described in a previous study, in which good inter-rater and intrarater reliability was shown compared with readings by a musculoskeletal radiologist.[20] For the MOON cohort, shoulder MRI scans were read in a standardized way by consensus between a trained senior orthopedic resident and a shoulder attending. Rotator cuff tear size was assessed in the transverse and longitudinal planes. The cross-sectional area of the tear size was then calculated by taking the product of the transverse and longitudinal tear sizes for the 2 largest tears. FI was evaluated based on fatty streaks within the muscle belly observed on a T1-weighted oblique sagittal image. It was graded as described by Goutallier et al.[14]: grade 0, no fat; grade 1, thin streaks of fat; grade 2, less fat than muscle; grade 3, equal amounts of fat and muscle; and grade 4, more fat than muscle. FI was assessed for all 4 rotator cuff muscles irrespective of the tendon that was torn. The highest FI grade for 1 of the 4 rotator cuff muscles was recorded for each patient. For the purposes of this analysis, the Goutallier grade was dichotomized to indicate the absence of FI (grade 0) as controls and the presence of any infiltration (grade $\geq$ 1) as cases.

Statistical analysis

We used multivariable logistic regression to evaluate the relationship between BMI and the presence of FI while adjusting for participant's age at MRI, sex, and duration of shoulder symptoms, as well as the cross-sectional area of the tear. BMI was assessed as a continuous variable and as a categorical variable, according to modified World Health Organization categories (<25 kg/m^2 [reference category; normal BMI], 25-30 kg/m^2 [overweight], or >30 kg/m^2 [obese]). Each cohort was analyzed separately, and resulting effect estimates were combined using inverse-variance weighted fixed-effects meta-analysis to avoid confounding due to cohort assignment. As a secondary analysis, we also evaluated the relationship between sex and FI using the same multivariable adjusted models mentioned earlier and performed meta-analysis for corresponding estimates. We conducted several sensitivity analyses in the ROW cohort to evaluate the robustness of the results and to seek further insight into the relationship between BMI, sex, and FI. We evaluated the association between BMI and FI with and without adjustment for covariates while varying the definition of FI on the Goutallier FI grading scale from grade 1 or higher to grade 2 or higher. To further evaluate how the relationship between BMI and FI is affected by the presence of a tear and whether the association between BMI and a tear is independent of tear presence, we constructed unadjusted and multivariable models of the supraspinatus, infraspinatus, subscapularis, and teres minor tendons separately. Multivariable models included FI (present or absent) of the specific tendon as the outcome (eg, FI of the supraspinatus) and tear thickness of that specific tendon (no tear [reference], partial-thickness tear, and full-thickness tear), BMI (continuous or categorical), participant's age at baseline, and sex as the independent variables. These models yielded effect estimates for the association between tear thickness and FI with and without adjustment for BMI, as well as for the association between BMI and FI with and without adjustment for the presence of a tear. The teres minor tendons had no tears, and multivariable models only included age, sex, and BMI as the independent variables. Sensitivity analyses were not possible in the MOON cohort because of the small number of FI events. Odds ratios (ORs) and 95% confidence intervals (CIs) are presented. Analyses were conducted in R version 4.0.2 (2020) (R Foundation for Statistical Computing, Vienna, Austria) and Stata (StataCorp, College Station, TX, USA).

Results

Approximately half the patients were female and one-third of rotator cuff tears had FI of the rotator cuff in both cohorts (MOON, 27 of 80 patients; ROW, 57 of 158 patients). In both cohorts, participants with FI were older on the date of MRI than those without FI and were more likely to be female, to be obese, and to have had tears for >12 years (Table I).

In our assessment of BMI as a continuous measure and FI, every 5-unit increase in BMI was associated with a 45% increased odds of FI (OR, 1.449; 95% CI, 0.859-2.447) in MOON patients and a 28% increased odds in ROW patients (OR, 1.282; 95% CI, 0.83-1.99), with a final meta-analysis OR of 1.351 (95% CI, 0.965-1.892) (Table II).). When BMI < 25 kg/m^2 was used as the referent category, being overweight was associated with a 2.3-fold increased odds of FI (meta-analysis OR, 2.3; 95% CI, 0.77-7.29) and being obese was associated with a 3.28-fold increased odds of FI (meta-analysis OR, 3.28; 95% CI, 1.16-9.25) (Table II). For the individual cohorts, being overweight as compared with having a BMI < 25 kg/m^2 was associated with a 7.13-fold increased odds of FI in the MOON cohort and a 1.097-fold increased odds of FI in the ROW cohort. This difference in ORs is likely a result of the smaller number of patients with FI in the overweight category in the MOON cohort as compared with the ROW cohort. Compared with men, women were 4.9 times as likely to have FI (meta-analysis OR, 4.91; 95% CI, 2.06-11.69), with a consistently positive direction of association in both cohorts (Table II).

Sensitivity analyses

In sensitivity analyses performed in the ROW cohort, changing the definition of FI to include only individuals with grade 2 FI or higher on the Goutallier scale showed that associations between BMI and FI were stronger with the magnitudes of the ORs being larger with the new

Table I Characteristics of participants in MOON and ROW cohorts with magnetic resonance images of rotator cuff

Characteristics	MOON			ROW		
	n	No FI (n = 53)	FI (n = 27)	n	No FI (n = 106)	FI (n = 60)
BMI, kg/m^2	80					
Q1, Q2, Q3		23, 25, 30	25, 29, 34		25, 28, 32	26, 29, 33
Mean (SD)		27.5 (5)	30 (6)		29 (6)	30 (5)
BMI by category	80			158		
<25 kg/m^2		42% (22)	22% (6)		23% (24)	15% (9)
25-30 kg/m^2		32% (17)	33% (9)		30% (31)	39% (23)
>30 kg/m^2		26% (14)	44% (12)		38% (41)	43% (26)
Missing		—	—		10% (10)	3% (2)
Age, yr	80					
Q1, Q2, Q3		55, 61, 69	59, 61, 69		53, 60, 67	60, 64, 69
Mean (SD)		62 (10)	65 (9)		61 (9)	64 (7)
Cross-sectional area, cm^2	80			149		
Q1, Q2, Q3		1, 2, 4	4, 5, 7		0, 0.4, 2.3	3.1, 13.3, 39.8
Mean (SD)		3 (3)	5 (3)		2.4 (4.6)	23.6 (24.0)
Sex	80			158		
Female		38% (20)	74% (20)		44% (47)	46% (26)
Male		62% (33)	26% (7)		56% (59)	54% (34)
Duration of shoulder symptoms, yr*	80			158		
<3		32% (17)	15% (4)		20% (21)	23% (14)
4-6		17% (9)	18% (5)		35% (37)	12% (7)
7-11		15% (8)	18% (5)		20% (21)	17% (10)
≥12		36% (19)	48% (13)		22% (24)	35% (21)
Missing		—	—		3% (3)	13% (8)

MOON, Multicenter Orthopaedic Outcomes Network; *ROW*, Rotator Cuff Outcomes Workgroup; *FI*, fatty infiltration; *BMI*, body mass index; *Q1*, quartile 1; *Q2*, quartile 2; *Q3*, quartile 3; *SD*, standard deviation.

* Prior to presentation.

Table II Associations evaluating BMI and sex in relation to fatty infiltration in MOON and ROW cohorts

Variable	MOON		ROW		Meta-analysis	
	OR	95% CI	OR	95% CI	OR	95% CI
BMI						
BMI (continuous)	1.077	0.970-1.196	1.051	0.963-1.148	1.062	0.993-1.136
BMI < 25 kg/m^2	1.000	Ref	1.000	Ref	1.000	Ref
BMI of 25-30 kg/m^2	7.132	1.236-41.156	1.097	0.254-4.748	2.369	0.770-7.291
BMI > 30 kg/m^2	3.498	0.743-16.465	3.116	0.773-12.558	3.281	1.164-9.248
Sex (female vs. male [Ref])	7.533	1.981-28.652	3.592	1.148-11.245	4.910	2.062-11.691

BMI, body mass index; *MOON*, Multicenter Orthopaedic Outcomes Network; *ROW*, Rotator Cuff Outcomes Workgroup; *OR*, odds ratio; *CI*, confidence interval; *Ref*, reference category. ORs and 95% CIs were estimated by logistic regression using BMI as a continuous variable or BMI as a categorical variable and sex, while adjusting for age at magnetic resonance imaging, cross-sectional area of the tear, and duration of the tear. Meta-analysis ORs (95% CIs) were estimated using inverse-variance weighted fixed-effects meta-analysis across the 2 studies.

definition (Table III). However, the substantial drop in FI cases (from 44 to 31) with the more stringent definition led to further loss of power and decreased precision in our estimates. Unadjusted and multivariable adjusted results were similar. In contrast to this finding, the association between sex and FI was starkly different, with no evidence of an increased association between female patients and FI (0 vs. grade 1 or higher) in the unadjusted model (OR, 0.95; 95% CI, 0.51-1.82) but a strong association in the multivariable adjusted model (OR, 3.59; 95% CI, 1.15-11.25) (Table III). This reversal in association compared with the unadjusted model was contributed by the adjustment for tear size (cross-sectional area of the tear). A similar reversal of association was seen when this association was assessed using grade 2 FI or higher as the outcome (Table III).

Table III Sensitivity analyses evaluating BMI and sex in relation to FI in ROW cohort

Variable	FI of grade 1 or higher			FI of grade 2 or higher		
	Cases/controls, n	OR	95% CI	Cases/controls, n	OR	95% CI
Unadjusted						
BMI						
BMI (continuous)	58/96	1.02	0.97-1.08	42/96	1.03	0.97-1.10
BMI < 25 kg/m^2	9/24	1.00	Ref	4/24	1.000	Ref
BMI of 25-30 kg/m^2	23/31	1.98	0.78-5.05	20/31	3.87	1.17-12.83
BMI > 30 kg/m^2	26/41	1.69	0.68-4.20	18/41	2.63	0.80-8.70
Sex (female vs. male [Ref])	58/96	0.95	0.51-1.82	42/96	0.70	0.33-1.46
Multivariable adjusted						
BMI						
BMI (continuous)	44/82	1.051	0.963-1.148	31/82	1.08	0.98-1.21
BMI < 25 kg/m^2	7/22	1.000	Ref	2/22	1.00	Ref
BMI of 25-30 kg/m^2	19/27	1.097	0.254-4.748	16/27	2.52	0.25-25.76
BMI > 30 kg/m^2	18/33	3.116	0.773-12.558	13/33	7.81	0.84-72.28
Sex (female vs. male [Ref])	44/82	3.592	1.148-11.245)	31/82	2.38	0.59-9.58

BMI, body mass index; *FI*, fatty infiltration (defined either as grade 1 or higher level on Goutallier scale or as grade 2 or higher level on Goutallier scale); *ROW*, Rotator Cuff Outcomes Workgroup; *OR*, odds ratio; *CI*, confidence interval; *Ref*, reference category. ORs and 95% CIs were estimated by logistic regression using BMI as a continuous variable or BMI as a categorical variable and sex, while adjusting for age at magnetic resonance imaging, cross-sectional area of the tear, and duration of the tear for the multivariable model. The unadjusted model only included BMI (continuous or categorical) or sex with FI.

In addition to evaluating FI as a composite and binary variable with FI defined as the presence of FI in any 1 (or more) of the 4 tendons, we assessed FI of each tendon separately (Tables IV and V). Irrespective of tear, FI was present in 30% of supraspinatus tendons, 27% of infraspinatus tendons, 16% of subscapularis tendons, and 10% of teres minor tendons evaluated (Table IV). Tears were present in 92% of the supraspinatus muscles evaluated; fewer were present in the infraspinatus (32%) and subscapularis (14%); and none were present in the teres minor tendons evaluated. Compared with not having a tear, having a full-thickness tear was associated with higher odds of FI in muscles where tears were present in one or more individuals, after adjustment for age, sex, and BMI: supraspinatus (OR, 3.93; 95% CI, 0.78-19.84), infraspinatus (OR, 27.22; 95% CI, 9.32-79.53), and subscapularis (OR, 5.64; 95% CI, 1.59-20.04) (Table IV). Similar results were observed for unadjusted and multivariable models (Table IV). Understanding the positive correlation between tears and FI in each tendon, we assessed whether BMI was associated with FI in each tendon with and without adjustment for a tear in the specific tendon (Table V). BMI was positively associated with FI with or without adjustment for tear thickness, with the multivariable adjusted OR for each unit increase in BMI (continuous) showing consistent associations in all 4 tendons: supraspinatus (OR, 1.04; 95% CI, 0.98-1.11); infraspinatus (OR, 1.09; 95% CI, 1.01-1.19); subscapularis (OR, 1.12; 95% CI, 1.03-1.21); and teres minor (OR, 1.11; 95% CI, 1.02-1.21) (Table V). Similar associations were observed in unadjusted models (Table V).

Discussion

Considering the limited evidence about the relationship between obesity and FI in the literature,[8,28,33] we performed a cross-sectional evaluation of the relationship between BMI and FI in individuals with rotator cuff tears from 2 independent cohorts. We found that obesity was associated with substantially higher odds of having FI in both cohorts after adjusting for age, sex, and tear characteristics including tear size and tear duration. The association between BMI and FI was similar when we changed the definition of FI to a more clinically relevant threshold of grade 2 or higher on the Goutallier grading scale. Women had substantially higher odds of FI than men after adjustment for confounding and mediating variables.

To our knowledge, only 3 other studies have reported on the association between measures of obesity and FI.[8,28,33] Lee et al[28] measured the fat fraction in the supraspinatus, infraspinatus, subscapularis, and teres minor muscle groups in 182 men and women presenting with shoulder problems including rotator cuff tears. They reported a positive association between BMI and fat fraction in multivariable adjusted linear regression models for each of the 4 muscle groups evaluated. Although the study adjusted for the presence of tears, the inclusion of individuals with and without tears could have potentially biased effect estimates between BMI and fat fraction because FI is far more prevalent in patients with tears than in those without tears. In agreement with Lee et al, our study found that the

Table IV Evaluation of relationship between tear thickness and FI by rotator cuff tendon location in ROW cohort

Tear location and thickness	n (%)	Goutallier FI grade, n (%)					Unadjusted OR (95% CI)	Adjusted OR (95% CI)
		0	1	2	3	4		
Supraspinatus								
No tear	13 (8)	11 (84.6)	0 (0.0)	1 (7.7)	1 (7.7)	0 (0.0)	1.0 (Ref)	1.00 (Ref)
Partial	53 (35)	48 (90.6)	4 (7.5)	0 (0.0)	1 (1.9)	0 (0.0)	0.57 (0.10-3.35)	0.51 (0.08-3.17)
Full	100 (65)	57 (57.0)	15 (15.0)	11 (11.0)	4 (4.0)	13 (13.0)	4.15 (0.87-19.70)	3.93 (0.78-19.84)
All	166 (100)	116 (69.9)	19 (11.5)	12 (7.2)	6 (3.6)	13 (7.8)	—	—
Infraspinatus								
No tear	112 (68)	100 (89.3)	9 (8.0)	2 (1.8)	1 (0.9)	0 (0.0)	1.00 (Ref)	1.00 (Ref)
Partial	12 (7)	10 (83.34)	1 (8.3)	0 (0.0)	1 (8.3)	0 (0.0)	1.67 (0.33-8.52)	0.73 (0.11-4.87)
Full	41 (25)	11 (26.8)	6 (14.6)	9 (22.0)	3 (7.3)	12 (29.3)	22.73 (9.11-56.70)	27.22 (9.32-79.53)
All	165 (100)	121 (73.3)	16 (9.7)	11 (6.7)	5 (3.0)	12 (7.3)	—	—
Subscapularis								
No tear	141 (86)	124 (87.9)	8 (5.7)	2 (1.4)	2 (1.4)	5 (3.6)	1.00 (Ref)	1.00 (Ref)
Partial	8 (5)	6 (75.0)	1 (12.5)	1 (12.5)	0 (0)	0 (0)	2.43 (0.45-13.03)	4.19 (0.60-29.18)
Full	15 (9)	8 (53.3)	1 (6.7)	1 (6.7)	4 (26.6)	1 (6.7)	6.38 (2.05-19.84)	5.64 (1.59-20.04)
All	164 (100)	138 (84.1)	10 (6.1)	4 (2.4)	6 (3.7)	6 (3.7)	—	—
Teres minor								
No tear	164 (100)	148 (90.2)	9 (5.5)	1 (0.6)	1 (0.6)	5 (3.1)	—	—

FI, fatty infiltration; *ROW*, Rotator Cuff Outcomes Workgroup; *OR*, odds ratio; *CI*, confidence interval; *Ref*, reference category. ORs were computed from logistic regression models for the association between tear thickness (no tear as reference group) and FI (grade ≥ 1). Unadjusted ORs represent models with only tear thickness as the independent variable; adjusted ORs represent models that were additionally adjusted for BMI, sex, and participant age at baseline.

Table V Evaluation of relationship between BMI and FI by rotator cuff tendon location in ROW cohort

Tear location and BMI	FI/no FI	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Supraspinatus			
BMI (continuous)	49/105	1.02 (0.96-1.08)	1.04 (0.98-1.11)
BMI $<$ 25 kg/m^2	7/26	1.00 (Ref)	1.00 (Ref)
BMI of 25-30 kg/m^2	22/32	2.55 (0.94-6.91)	5.26 (1.60-17.33)
BMI $>$ 30 kg/m^2	20/47	1.58 (0.59-4.23)	3.06 (0.98-9.55)
Infraspinatus			
BMI (continuous)	44/109	1.06 (1.00-1.12)	1.09 (1.01-1.19)
BMI $<$ 25 kg/m^2	4/29	1.00 (Ref)	1.00 (Ref)
BMI of 25-30 kg/m^2	18/36	3.63 (1.10-11.90)	3.20 (0.66-15.66)
BMI $>$ 30 kg/m^2	22/44	3.63 (1.13-11.61)	7.10 (1.41-35.85)
Subscapularis			
BMI (continuous)	55/127	1.08 (1.01-1.16)	1.12 (1.03-1.21)
BMI $<$ 25 kg/m^2	1/32	1.00 (Ref)	1.00 (Ref)
BMI of 25-30 kg/m^2	11/42	8.38 (1.03-68.31)	5.90 (0.64-53.95)
BMI $>$ 30 kg/m^2	13/53	7.85 (0.98-62.87)	8.99 (1.07-75.69)
Teres minor			
BMI (continuous)	16/136	1.08 (1.00-1.17)	1.11 (1.02-1.21)
BMI $<$ 25 kg/m^2	2/31	1.00 (Ref)	1.00 (Ref)
BMI of 25-30 kg/m^2	4/49	1.27 (0.22-7.32)	1.70 (0.28-10.52)
BMI $>$ 30 kg/m^2	10/56	2.77 (0.57-13.44)	3.94 (0.76-20.60)

BMI, body mass index; *FI*, fatty infiltration defined as absent (grade 0 on Goutallier scale) and present (Goutallier grades 1-4 as infiltration); *ROW*, Rotator Cuff Outcomes Workgroup; *OR*, odds ratio; *CI*, confidence interval; *Ref*, reference category. ORs were computed for BMI measures and FI with and without multivariable adjustment by tendon location. For the supraspinatus, infraspinatus, and subscapularis, the multivariable models were adjusted for age at magnetic resonance imaging, sex, and tear thickness in the corresponding tendon (none, partial-thickness tear, or full-thickness tear). The multivariable model for the teres minor did not adjust for tears because there were no tears.

positive associations between tear size and FI and between BMI and FI are independent of each other as shown by the persistence of associations after mutually adjusting for each other. These associations were consistent across all 4 tendons evaluated separately. Similarly to Lee et al, we did not find any tears in the teres minor tendon and observed a positive association between BMI and FI. Yet, we are not able to state whether this is independent of tears as the influence of a tear of an adjacent or nearby tendon on FI of the tendon in question cannot be discounted fully. A limitation of the study by Lee et al and our study is the cross-sectional design in which information on BMI and FI are abstracted simultaneously, making it difficult to draw inferences regarding temporality. It is not clear whether an elevated BMI leads to FI in individuals with tears or whether the observation between BMI and FI is coincidental, owing to the presence of tears.

The 2 other studies that evaluated this association between BMI and FI were performed in individuals without rotator cuff tears.[8,33] The observation of a positive association between BMI and FI by both studies suggests that the relationship between obesity and FI may be independent of tears.

FI is histologically associated with increased interstitial connective tissue that is vascular with high macrophage density. Fat accumulation occurs at the surface of the muscle and within the sarcoplasm of muscle fibers. Obesity-induced alterations may promote FI through mechanisms that remain not fully understood. Matson et al[33] postulated that alterations in signaling pathways of proteins involved in rotator cuff muscle homeostasis such as protein kinase B (Akt) and mammalian target of rapamycin (mTOR)[40] may result in activation of genes that enhance protein breakdown and activate adipogenic changes mediated by sterol regulating element-binding protein 1 (SREBP1) and fibrotic changes mediated by transforming growth factor β (TGF-β).[30] This may promote differentiation of preadipocytes into adipocytes[29] via peroxisome proliferator-activated receptor γ (PPARγ),[24] which is linked to obesity.[11,41]

It is well understood that the functional outcomes of individuals who undergo surgical repair for rotator cuff tears are better in the absence of FI.[13,14,26,31,32,36,42,43,45] It is not known if weight reduction can reduce FI. If obesity is causally associated with FI, then understanding whether FI can be reversed in part by losing body weight (through fat loss) has potential implications for patient care, in which a weight loss regimen prior to surgery may be used to reduce FI. Our study does not provide data on this issue, which needs further research.

We also evaluated the relationship between sex and FI and found that women were more likely to have FI than men after adjustment for age, BMI, tear size, and tear duration. This association was present in both cohorts, ROW and MOON. Lee et al[28] reported a higher fat fraction in the supraspinatus, infraspinatus, and subscapularis in female patients as compared with male patients after adjustment for confounders. To find potential explanations for this observed association, we assessed the relationship between sex and FI with and without adjustment for covariates in the ROW cohort. We only observed a statistically significant increased odds of FI in women compared with men when we evaluated this association in a multivariable model. This association was absent in a model that included only sex and FI, suggesting that 1 or more of the variables that we adjusted for were strongly correlated with sex and FI. With the exception of aging, all other factors that we adjusted for are potential mediators of the association between sex and FI rather than confounders. Further evaluation of data showed that women in our study, on average, had a smaller tear size (cross-sectional mean, 7.88 cm^2 [standard deviation, 14.9 cm^2]) than men (cross-sectional mean, 13.24 cm^2 [standard deviation, 20.96 cm^2]). Because women were less likely to have larger tears and because larger tears are associated with higher degrees of FI, adjusting for this mediating variable necessarily generates a positive association between sex and FI. Therefore, the results should be carefully interpreted, indicating that women are more likely to have FI than men only when the size of the tear is held constant on average. Barry et al[1] reported a 1.7 times increased odds of having higher grades of FI for women than for men. Sex differences in body fat composition are established, with women having approximately 10% higher body fat compared with men for the same BMI.[12,17,25,44] Women have a lower intra-abdominal fat mass than men on average and have a higher amount of subcutaneous white adipose tissue in the abdominal and gluteofemoral areas than men.[2,5,6,38] Whether women are more likely to have background FI than men, independent of tears, and whether this association is mediated by differences in fat composition and distribution are questions better addressed in a larger sample of men and women who do not have rotator cuff tears than in our present study, which only assessed FI in men and women with tears. Although the mechanism is not entirely clear, it is possible that body fat composition differences and hormonal differences between men and women contribute toward a higher presence of FI of the rotator cuff in women. This may also be relevant to shoulder pain and functional outcomes after rotator cuff surgery where sex differences were reported in the early postoperative recovery period. Women reported greater pain[3,4] and lower American Shoulder and Elbow Surgeons scores[4,37] than men. If women have a higher propensity toward FI, a well-established factor for poor postsurgical outcomes, this may in part explain suboptimal outcomes in women as compared with men that have been previously attributed to differences in pain perception and societal expectations.

Conclusion

FI is one of the most important prognostic factors for outcomes after rotator cuff surgery. However, data on the relationship between FI and obesity and between FI and sex are limited. We found that among patients with rotator cuff tears, obese patients had a significantly higher likelihood of FI. Sex was also significantly associated with FI, with female patients having substantially higher odds of FI than male patients. The impact of modifying BMI in patients with rotator cuff tears on FI needs to be further studied. If women are more likely to have FI of the rotator cuff than men, as our results suggest, this may also explain the suboptimal outcomes of rotator cuff surgery and higher pain levels in female patients than in male patients. Supported by further investigations, these findings may lead to personalized care for rotator cuff tear patients before and after surgery and improvements in surgical outcomes.

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Conflicts of interest: Laurence D. Higgins is an employee of Arthrex.

Robert G. Marx is an author for Demos Health; receives book royalties from Demos Health and Springer; is an editorial board member of the *Journal of Bone & Joint Surgery*; is a science advisory board member of Mend; has ownership interest in Mend; and is an editor for Springer.

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