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# Obesity is associated with muscle atrophy in rotator cuff tear

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## ABSTRACT

**Objective** The primary goal of this study is to evaluate the relationship between Body Mass Index (BMI) and muscle atrophy in individuals with rotator cuff tears.

**Methods** This study consists of patients with rotator cuff tears identified by MRI from two independent cohorts, the Rotator Cuff Outcomes Workgroup (ROW) and the Multicenter Orthopaedic Outcomes Network (MOON). Presence of atrophy (yes/no) and severity of atrophy (as an ordinal variable) were assessed on MRI by expert physicians. We used multivariable regression models to evaluate the relationship between BMI and muscle atrophy while adjusting for age and sex in each study, conducted sensitivity analyses for full-thickness tear and combined results using inverse variance-weighted meta-analysis.

**Results** A total of 539 patients (MOON=395, ROW=144) from the combined cohorts had MRI data available on muscle atrophy. Among these patients, 246 (46%) had atrophy of at least one of the muscles of the rotator cuff and 282 (52%) had full-thickness tears. In meta-analysis across both cohorts, each 5 kg/m<sup>2</sup> increase in BMI was associated with a 21% (aOR=1.21, 95% CI=1.02, 1.43) increased odds of having muscle atrophy among individuals with any tear size, and 36% (aOR=1.36, 95% CI=1.01–1.81) increased odds among individuals with full-thickness tear.

**Conclusions** Higher BMI was associated with significantly higher odds of muscle atrophy in patients with rotator cuff tears. More study is needed to understand why and how this relationship exists, as well as whether interventions to reduce BMI may help improve outcomes for these patients.

**Level of Evidence** III.

## INTRODUCTION

Rotator cuff tears are considered a common cause of shoulder pain and are among the most common shoulder pathologies, affecting approximately 40% of the population over 60 years of age.<sup>1–3</sup> The chronic shoulder pain resulting from randomised controlled trial (RCT) can result in daily suffering leading to limited range of motion, muscle weakness and inability to perform even simple daily

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Muscle atrophy is a common consequence of rotator cuff tear and one of the most important histopathological changes that is a well-known predictor of surgical outcomes, yet not all patients with cuff tear develop muscle atrophy and it is not known why.
- ⇒ Obesity is a well-known risk factor for degenerative rotator cuff tears, with several studies linking higher Body Mass Index (BMI) to increased risk of rotator cuff tear.

## WHAT THIS STUDY ADDS

- ⇒ Higher BMI was associated with significantly higher odds of muscle atrophy.
- ⇒ The association between BMI and muscle atrophy is even more pronounced in individuals with full-thickness tear.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, POLICY OR PRACTICE

- ⇒ The positive association between BMI and muscle atrophy identified in this study suggests that it is possible that efforts to modify BMI in patients with rotator cuff pathology could mitigate muscle loss and even potentially help rebuild lost muscle mass.
- ⇒ This work paves the way for future efforts to understand the causal pathway and mechanisms for the association of BMI with muscle atrophy and interventions to reduce it, which in turn will likely help improve clinical outcomes.

tasks such as combing one's hair or brushing one's teeth.<sup>3–6</sup>

Muscle atrophy is a common consequence of RCT, particularly in cases where the tear is chronic or longstanding, and can lead to loss of function, chronic pain and decreased quality of life in affected individuals. Advanced muscle atrophy is associated with worse surgical outcomes, higher rates of retear and poorer postoperative strength and range of motion.<sup>7–13</sup> Thus, clinicians often rely on measures of muscle atrophy in MRI

to influence their decision making regarding surgical vs conservative management.<sup>11 14</sup>

Obesity is a well-known risk factor for degenerative rotator cuff tears, with several studies linking higher Body Mass Index (BMI) to increased risk of rotator cuff tear.<sup>15–22</sup> The mechanisms by which obesity contributes to rotator cuff tear are not fully understood, but it is thought to be related to musculotendinous changes, increased mechanical loading on the shoulder joint and alterations in muscle function and metabolism. In particular, obesity is associated with alterations in adipokine secretion,<sup>23</sup> insulin resistance and chronic low-grade inflammation,<sup>24</sup> all of which can contribute to muscle atrophy and impaired muscle function. Additionally, recent work suggests a potential genetic association as studies have found myogenic, adipogenic and ‘atrophy’ genes that are correlated with increased muscle atrophy in rotator cuff tears.<sup>25</sup>

Though prior work for our group has found that obesity is correlated with increased fatty infiltration of the rotator cuff, a distinct muscle abnormality found in individuals with tears which is often found in conjunction with muscle atrophy, to our knowledge, no studies to date have identified modifiable physical risk factors for muscle atrophy. The objective of this study is to evaluate the relationship between BMI and muscle atrophy of rotator cuff muscles in two well-characterised cohorts of patients with rotator cuff tears.

## METHODS

### Patient populations

This study consists of two independent cohorts, the Rotator Cuff Outcomes Workgroup (ROW) cohort and the Multicenter Orthopaedic Outcomes Network (MOON) cohort.

**ROW cohort:** This cohort recruited 390 patients with shoulder pain over the age of 45 from sports or shoulder clinics in three academic settings and one community setting between February 2011 and June 2015.<sup>26–28</sup> From the ROW cohort, this study included only the 144 patients that had symptomatic rotator cuff tears. Tears were confirmed with MRI and symptomatic was defined as at least 4 weeks of shoulder pain or dysfunction. Patients were excluded if they had prior shoulder surgery (on the index shoulder), current shoulder fracture or active cervical radiculopathy (elicited as neck pain radiating to the shoulder, arm and/or hand). All patients provided informed consent.

**MOON cohort:** The MOON Shoulder Group consists of 16 fellowship-trained orthopaedic surgeons and research personnel from 10 different locations across the USA, including both academic and private practice settings. This cohort recruited 452 patients from January 2007 to January 2011 with MRI-confirmed rotator cuff tear.<sup>29</sup> Patients aged 18 to 100 years who had a full-thickness atraumatic symptomatic rotator cuff tear confirmed by MRI were eligible for participation. From the MOON cohort, this study included 395 patients with

MRI-confirmed rotator cuff tears. Patients were excluded if they had pain caused by a precipitating injury, pain linked to cervical pathology, scapular pain, previous shoulder surgery, glenohumeral arthritis, inflammatory arthritis, adhesive capsulitis, previous proximal humeral fracture, symptomatic contralateral rotator cuff tear or dementia.

### Structured assessments

For both cohorts, at the time of recruitment, patients filled out a baseline questionnaire which provided information on basic demographics, participant characteristics and details related to rotator cuff pathology.

### Assessment of Body Mass Index (BMI)

BMI was calculated from patient’s self-reported height and weight. If height or weight was missing, they were abstracted from the patient’s electronic medical record using measures from visits prior to and inclusive of the recruitment visit. In this study, results are reported for BMI continuously and, for clinical applicability, categorically and dichotomously. BMI was modelled categorically using the modified-WHO BMI categories: normal weight:  $<25 \text{ kg/m}^2$ ; overweight:  $25 \text{ kg/m}^2$ – $29.9 \text{ kg/m}^2$ ; and obese:  $\geq 30 \text{ kg/m}^2$ .

### Assessment of muscle atrophy, tear size and tear thickness

In both cohorts, shoulder MRIs were read by fellowship-trained attending physicians, who are shoulder experts. Characteristics extracted for this study include muscle atrophy, tear thickness and tear sizes. In previous studies, the methodology of the ROW MRI reviews was described and found to have good inter-rater and intra-rater reliability compared to musculoskeletal radiologist readings.<sup>30</sup>

For the MOON cohort, an MRI assessment was performed by the recruiting shoulder surgeon at the time of patient recruitment. Initial MRI assessment included grading of muscle atrophy, however, did not include tear size. Therefore, for patients identified by the MOON cohort with MRI of sufficient quality to permit assessment of longitudinal and transverse tear size ( $n=184$ ), tear size was measured post-hoc through consensus between a trained senior orthopaedic resident and a shoulder attending. This was done in a centralised manner by collecting MRI’s from all recruitment sites for the MOON cohort. We could only obtain 184 MRI’s post-hoc to measure tear size. Additional details of MRI classification for the MOON cohort have been published in prior studies.<sup>27 29</sup>

Rotator cuff tear size was assessed in the transverse and longitudinal planes. Tear size was graded as small ( $<1 \text{ cm}$ ), medium ( $1$ – $3 \text{ cm}$ ) and large/massive ( $>3 \text{ cm}$ ) in accordance with current radiological classification practice.<sup>31</sup> Cross-sectional area ( $\text{cm}^2$ ) of tear size was calculated by taking the product of transverse and longitudinal tear sizes for the two largest tears.

Tear thickness was assessed with T2 and T1-weighted MRI consistent with prior studies.<sup>32 33</sup> Full-thickness tears consisted of complete disruption of all tendon fibres, as determined by isointense signal compared with fluid on the T2-weighted images extending from articular to bursal surface on one or more images. Partial tears consisted of fluid intensity that was only in contact with one surface, or incomplete discontinuity of some (but not all) tendon fibres. Mild fraying in isolation did not constitute partial-thickness tear.

Muscle atrophy was assessed for each of the four muscles of the rotator cuff and evaluated for degree of atrophy in each muscle-belly observed on a T1-weighted oblique sagittal image. For the ROW cohort, muscle atrophy was graded in accordance with the scale by Warner *et al*<sup>34</sup> as grade 1, no atrophy; grade 2, mild; grade 3, moderate; and grade 4, severe. For the MOON cohort, muscle atrophy was graded as grade 0, no atrophy; grade 1, 25% atrophy; grade 2, 50% atrophy; grade 3, 75% atrophy; and grade 4, complete atrophy. In order to merge data from both cohorts and perform a meta-analysis, atrophy scales were harmonised to the ROW scale such that grade 0 in the MOON scale was recategorised as the new grade 1; grade 1 in the MOON scale was recategorised as the new grade 2; grade 2 in the MOON scale was recategorised as the new grade 3; and grades 3 and 4 in the MOON scale were recategorised as the new grade 4. In this study, we report and assess atrophy quantitatively, as a sum of atrophy scores across all muscles, and dichotomously, as presence of any atrophy in any muscle. The sum of muscle atrophy is a composite score that captures two characteristics, the severity of tear and the number of muscles torn. Therefore, this metric could result in an equal score for individuals with a high degree of tear in relatively few muscles and individuals with low degree of tear but in more muscles.

### Statistical analysis

Patient demographics and clinical characteristics were first compared between the two study cohorts, then within each cohort compared by muscle atrophy status as median with interquartile range for continuous variables and frequency with percentages for categorical variables. We estimated the association between BMI and presence of muscle atrophy with univariate and multivariable-adjusted regression models within each study cohort. We then used inverse variance-weighted meta-analysis to summarise results across studies. Because of potentially meaningful demographic differences between the two cohorts, meta-analysis was performed over pooled analysis.

In the primary multivariable logistic regression models, we adjusted for patient's age and sex. Given that tear size was missing in a substantial number of patients, we also included a sensitivity analysis for tear size by conducting a pre-planned subgroup analysis where only patients with full-thickness rotator cuff tear were included, and further adjusting for cross-sectional area of the tear. In all

primary analyses, muscle atrophy status (having atrophy vs not having atrophy) was analysed with binary logistic regression models, where BMI was analysed both continuously (linear) and categorically (WHO category). In sensitivity analyses, similar approach was used except the muscle atrophy scores were analysed with ordinal logistic regression models. We report OR or adjusted OR, along with the 95% CIs and p values. From both approaches, an OR greater than 1 indicates a positive association between the presence (logistic regression) or severity (ordinal logistic regression) of muscle atrophy and increase in BMI (analysed continuously) or higher BMI category as compared with normal. A two-sided p value less than 0.05 was considered statistically significant. All analyses were performed using software R V.4.3.

### Patient and public involvement

No patients or any members of the public were involved in the design, conduct, reporting or dissemination plans of the research.

### Equity, diversity and inclusion statement

In pursuit of equity, diversity and inclusion, our study upholds a commitment to ensuring representation and inclusivity across various facets. First, our authorship team embodies a mosaic of professional backgrounds and career stages, ranging from medical student trainees to esteemed department heads. Notably, our team also reflects demographically diverse authorship with individuals from various racial and ethnic backgrounds, four different countries and three authors who identify as female. Moreover, our team reflects a diverse array of professional backgrounds, including MDs, PhDs and other disciplines. This study benefits from a globally diverse authorship, drawing expertise from 17 institutions and several different continents. Additionally, our patient cohort mirrors this diversity, representing 14 different institutions, encompassing a spectrum of racial, demographic, socio-economic, gender, occupational and geographical backgrounds. Finally, in line with our commitment to equity, distinct statistical analyses were conducted to scrutinise potential sex disparities, ensuring a comprehensive exploration of rotator cuff muscle atrophy.

## RESULTS

### Demographics

Demographic data across both cohorts is comparable, with almost identical average age, BMI and rate of diabetes. Both cohorts have an average age of approximately 60 years old, almost equal distribution of male and female patients, and average BMI of about 30 kg/m<sup>2</sup>. However, presence of atrophy was different in the two cohorts, with the ROW cohort having a lower percentage of atrophy (28%) as compared with the MOON cohort (52%) (<0.001). This was expected because the ROW cohort had some individuals with partial thickness tears 31.2% (69%) and the MOON cohort only included

**Table 1** Descriptive statistics by study

| Characteristic                          | N   | MOON n=395        | ROW n=144         |
|---|-----|-------------------|-------------------|
| Presence of atrophy                     | 539 |                   |                   |
| No                                      |     | 190 (48.1%)       | 103 (71.5%)       |
| Yes                                     |     | 205 (51.9%)       | 41 (28.5%)        |
| Atrophy score                           | 539 |                   |                   |
| 0                                       |     | 190 (48.1%)       | 103 (71.5%)       |
| 1                                       |     | 80 (20.3%)        | 6 (4.2%)          |
| 2                                       |     | 51 (12.9%)        | 10 (6.9%)         |
| 3                                       |     | 27 (6.8%)         | 7 (4.9%)          |
| 4+                                      |     | 47 (11.9%)        | 18 (12.5%)        |
| Age                                     | 539 | 62.0 (56.0, 69.0) | 63.1 (55.9, 68.0) |
| Sex                                     | 539 |                   |                   |
| Female                                  |     | 190 (48.1%)       | 62 (43.1%)        |
| Male                                    |     | 205 (51.9%)       | 82 (56.9%)        |
| Race                                    | 526 |                   |                   |
| White                                   |     | 336 (87.0%)       | 126 (90.0%)       |
| Black                                   |     | 33 (8.5%)         | 12 (8.6%)         |
| Other                                   |     | 17 (4.4%)         | 2 (1.4%)          |
| BMI                                     | 539 | 28.4 (24.6, 32.2) | 28.6 (25.8, 32.4) |
| BMI category                            | 539 |                   |                   |
| 18.5~25                                 |     | 107 (27.1%)       | 31 (21.5%)        |
| 25~30                                   |     | 138 (34.9%)       | 53 (36.8%)        |
| ≥ 30                                    |     | 150 (38.0%)       | 60 (41.7%)        |
| Diabetes                                | 530 |                   |                   |
| No                                      |     | 336 (86.8%)       | 127 (88.8%)       |
| Yes                                     |     | 51 (13.2%)        | 16 (11.2%)        |
| Cross-Sectional Area (cm <sup>2</sup> ) | 279 | 2.7 (1.4, 5.2)    | 3.0 (1.6, 8.0)    |
| Tear thickness                          | 539 |                   |                   |
| Full                                    |     | 395 (100.0%)      | 99 (68.8%)        |
| Partial                                 |     | 0 (0.0%)          | 45 (31.2%)        |

BMI, Body Mass Index; MOON, Multicenter Orthopaedic Outcomes Network; ROW, Rotator Cuff Outcomes Workgroup.

patients with full-thickness tears (table 1). We opted to use meta-analysis rather than pooling as the preferred method of combining data across studies considering this major difference in tear characteristics.

### Characteristics by atrophy status

We further evaluated characteristics of participants by atrophy status, separately for the MOON and ROW cohorts. Across both cohorts, there was no meaningful difference in sex (MOON  $p=0.09$  and ROW  $p=0.81$ ), BMI (MOON  $p=0.44$  and ROW  $p=0.81$ ) or diabetes (MOON  $p=0.09$  and ROW  $p=0.76$ ) by atrophy status. In both cohorts, the median atrophy score per individual (as defined using the sum of atrophy scores across all

muscles for individuals with atrophy) was 2, with a right skewed distribution. While the MOON cohort contains only individuals with full-thickness tear, the ROW cohort consisted of all degrees of tear. In the ROW cohort, the majority of individuals had a full-thickness tear (68.8%,  $p<0.01$ ). In both cohorts, there was, however, a significant difference in cross-sectional area of the tear, with atrophic tears having larger cross-sectional areas ( $p<0.01$  for both MOON and ROW). Lastly, in both cohorts, those with atrophy were older on average than those without atrophy (MOON  $p<0.01$  and ROW  $p=0.02$ ) (table 2).

### Primary analyses

In our assessment of BMI as a continuous measure and atrophy as a binary variable, every 5 kg/m<sup>2</sup> increase in BMI was associated with a 29% increased odds of muscle atrophy (aOR=1.29; 95% CI=1.06, 1.56) in MOON and 2% increased odds in ROW (aOR=1.02; 95% CI=0.73, 1.42), with a final meta-analysis OR of 1.21 (aOR=1.21; 95% CI=1.02, 1.43). Results for separate analyses of BMI as a categorical variable, using BMI <25 as the referent category, align with prior analyses and similarly show a positive association between BMI and risk of atrophy (table 3).

### Sensitivity analyses

We conducted sensitivity analyses to evaluate the robustness of evidence. Because muscle atrophy is clinically graded, with higher numbers indicating more severe atrophy (indicating greater number of muscles involved and/or higher degree of tear), primary sensitivity analyses consisted of evaluating atrophy as an ordinal outcome (table 4). Regardless of BMI structure (continuous or categorical), the trends in effect of BMI on muscle atrophy were similar to those when atrophy was modelled dichotomously (Online supplemental tables 1 and 2).

Additionally, we conducted sensitivity analyses to evaluate for evidence of effect modification of sex. To that end, we conducted sex stratified analyses investigating the effect of BMI as a continuous and categorical variable on muscle atrophy in the MOON cohort. Analyses stratified by sex were not attempted within ROW due to the limited data. While there was no statistical evidence of effect modification in univariate analyses, the effect of BMI seemed to be stronger in men than in women, particularly in analyses adjusted for age. However, because of the small sample size, there is not enough evidence to conclusively suggest effect modification by sex (Online supplemental table 3).

Lastly, since one study noted potentially irreversible post-surgical muscle atrophy among patients with full-thickness tears,<sup>35</sup> we also conducted subgroup analyses consisting of individuals with full-thickness tears only. In those analyses, we adjusted for age and sex only, as well as age, sex and cross-sectional area of tear. Meta-analysis results from both adjusted full-thickness only models (with and without adjustment for cross-sectional area)

**Table 2** Descriptive statistics by atrophy status for study cohort

| Characteristics                         | MOON cohort |                      |                      | P value | ROW cohort |                      |                      | P     |
|---|-------------|----------------------|----------------------|---------|------------|----------------------|----------------------|-------|
|   | N           | No atrophy<br>n=190  | Atrophy<br>n=205     |         | N          | No atrophy<br>n=103  | Atrophy<br>n=41      |       |
| Age                                     | 395         | 59.0<br>(54.0, 63.0) | 66.0<br>(59.0, 74.0) | <0.01   | 144        | 62.7<br>(53.3, 67.2) | 64.4<br>(60.9, 68.6) | 0.02  |
| Sex                                     | 395         |                      |                      | 0.09    | 144        |                      |                      | 0.81  |
| Female                                  |             | 83 (43.7%)           | 107 (52.2%)          |         |            | 45 (43.7%)           | 17 (41.5%)           |       |
| Male                                    |             | 107 (56.3%)          | 98 (47.8%)           |         |            | 58 (56.3%)           | 24 (58.5%)           |       |
| Race                                    | 386         |                      |                      | 0.29    | 140        |                      |                      | 0.02  |
| White                                   |             | 167 (89.8%)          | 169 (84.5%)          |         |            | 88 (88.9%)           | 38 (92.7%)           |       |
| Black                                   |             | 12 (6.5%)            | 21 (10.5%)           |         |            | 11 (11.1%)           | 1 (2.4%)             |       |
| Other                                   |             | 7 (3.8%)             | 10 (5.0%)            |         |            | 0 (0.0%)             | 2 (4.9%)             |       |
| BMI                                     | 395         | 28.2<br>(24.4, 31.8) | 28.5<br>(24.8, 32.7) | 0.44    | 144        | 28.9<br>(25.4, 32.5) | 27.6<br>(26.0, 32.3) | 0.94  |
| BMI category                            | 395         |                      |                      | 0.81    | 144        |                      |                      | 0.15  |
| 18.5~25                                 |             | 53 (27.9%)           | 54 (26.3%)           |         |            | 25 (24.3%)           | 6 (14.6%)            |       |
| 25~30                                   |             | 68 (35.8%)           | 70 (34.1%)           |         |            | 33 (32.0%)           | 20 (48.8%)           |       |
| >= 30                                   |             | 69 (36.3%)           | 81 (39.5%)           |         |            | 45 (43.7%)           | 15 (36.6%)           |       |
| Diabetes                                | 387         |                      |                      | 0.09    | 144        |                      |                      | 0.76  |
| No                                      |             | 168 (89.8%)          | 168 (84.0%)          |         |            | 92 (89.3%)           | 35 (87.5%)           |       |
| Yes                                     |             | 19 (10.2%)           | 32 (16.0%)           |         |            | 11 (10.7%)           | 5 (12.5%)            |       |
| Thickness                               | 395         |                      |                      | NA      | 144        |                      |                      | <0.01 |
| Full                                    |             | 190 (100.0%)         | 205 (100.0%)         |         |            | 61 (59.2%)           | 38 (92.7%)           |       |
| Partial                                 |             | 0 (0%)               | 0 (0%)               |         |            | 42 (40.8%)           | 3 (7.3%)             |       |
| Cross-sectional area (cm <sup>2</sup> ) | 184         | 1.6<br>(1.0, 2.9)    | 5.0<br>(2.4, 6.8)    | <0.01   | 95         | 2.2<br>(0.9, 3.3)    | 8.3<br>(3.9, 15.2)   | <0.01 |

MOON, Multicenter Orthopaedic Outcomes Network; ROW, Rotator Cuff Outcomes Workgroup.

provide similar for estimates indicating that the association between BMI and muscle atrophy is independent of tear size (Online supplemental tables 1 and 2).

## DISCUSSION

In this study, we present findings from a cross-sectional evaluation of the relationship between obesity and muscle atrophy in individuals with rotator cuff tears from two independent cohorts. We found that, in both MOON and ROW cohorts, BMI was associated with an increased risk of muscle atrophy. However, this relationship reached statistical significance in the MOON cohort, and not in the ROW cohort, likely due to smaller sample size. In meta-analysis, BMI was positively associated with muscle atrophy for all combinations of continuous, categorical or ordinal modelling of exposures and outcomes, when adjusting for age and sex.

Further, we found that all observed associations were consistent among individuals with full-thickness tears even after adjustment for tear size. The clinical implications of this finding are important since they suggest a potential interplay between adiposity and the progression of muscle degeneration. Muscle atrophy and fatty

infiltration are the two most important histopathological changes that are well-known predictors of surgical outcomes,<sup>7-13</sup> where individuals with highly fatty, atrophic tears are often excluded as candidates for surgical repair.<sup>11 14</sup> Prior work from our group identified positive associations between female sex and obesity with fatty infiltration of the rotator cuff;<sup>27</sup> however, little research has been done on the association of obesity and muscle atrophy.

## Clinical implications

It is known that muscle atrophy worsens from time of injury to time of surgery,<sup>11</sup> but it is not yet established if this atrophy is reversible. One study out of South Korea found that, regardless of age, tear size or initial degree of atrophy, patients who underwent rotator cuff repair and were able to regain load-bearing status of their cuff were able to significantly improve their muscle size post-operatively.<sup>36</sup> This study, combined with the results of two prior studies,<sup>37 38</sup> indicates that muscle atrophy might be a reversible phenomenon. Therefore, the positive association between BMI and muscle atrophy identified in this study suggests that it is possible that efforts to modify

**Table 3** Adjusted associations between risk factors and muscle atrophy (binary)

|                              | MOON                                  |                            |      | ROW                                   |                     |      | Meta-analysis                         |                            |             |
|------------------------------|---------------------------------------|----------------------------|------|---------------------------------------|---------------------|------|---------------------------------------|----------------------------|-------------|
|                              | N <sub>Case</sub> /N <sub>Total</sub> | OR (95% CI)                | P    | N <sub>Case</sub> /N <sub>Total</sub> | OR (95% CI)         | P    | N <sub>Case</sub> /N <sub>Total</sub> | OR (95% CI)                | P           |
| BMI continuous               |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| Unadjusted                   |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| BMI (per five unit increase) | 205/395                               | 1.06 (0.90 to 1.25)        | 0.49 | 41/144                                | 1.01 (0.73 to 1.39) | 0.95 | 246/539                               | 1.05 (0.91 to 1.21)        | 0.52        |
| Adjusted*                    |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| BMI (per five unit increase) | 205/395                               | <b>1.29 (1.06 to 1.56)</b> | 0.01 | 41/144                                | 1.02 (0.73 to 1.42) | 0.91 | 246/539                               | <b>1.21 (1.02 to 1.43)</b> | <b>0.03</b> |
| BMI categorical              |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| Unadjusted                   |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| BMI <25                      | 54/107                                | ref                        |      | 6/31                                  | ref                 |      | 60/138                                | ref                        |             |
| 25–30                        | 70/138                                | 1.01 (0.61 to 1.67)        | 0.97 | 20/53                                 | 2.53 (0.88 to 7.22) | 0.08 | 90/191                                | 1.20 (0.76 to 1.89)        | 0.43        |
| >=30                         | 81/150                                | 1.15 (0.70 to 1.89)        | 0.58 | 15/60                                 | 1.39 (0.48 to 4.03) | 0.55 | 96/210                                | 1.19 (0.76 to 1.87)        | 0.45        |
| Adjusted*                    |                                       |                            |      |                                       |                     |      |                                       |                            |             |
| BMI <25                      | 54/107                                | ref                        |      | 6/31                                  | ref                 |      | 60/138                                | ref                        |             |
| 25–30                        | 70/138                                | 1.41 (0.77 to 2.58)        | 0.26 | 20/53                                 | 2.70 (0.90 to 8.17) | 0.08 | 90/191                                | 1.64 (0.97 to 2.78)        | 0.07        |
| >=30                         | 81/150                                | <b>2.12 (1.18 to 3.81)</b> | 0.01 | 15/60                                 | 1.47 (0.49 to 4.45) | 0.49 | 96/210                                | <b>1.96 (1.17 to 3.29)</b> | <b>0.01</b> |

\*Adjusted for age and sex.  
MOON, Multicenter Orthopaedic Outcomes Network; ROW, Rotator Cuff Outcomes Workgroup.

**Table 4** Adjusted associations between risk factors and muscle atrophy (ordinal)

|                              | MOON               |                            |             | ROW                |                     |      | Meta-analysis      |                            |             |
|------------------------------|--------------------|----------------------------|-------------|--------------------|---------------------|------|--------------------|----------------------------|-------------|
|                              | N <sub>Total</sub> | OR (95% CI)                | P           | N <sub>Total</sub> | OR (95% CI)         | P    | N <sub>Total</sub> | OR (95% CI)                | P           |
| BMI continuous               |                    |                            |             |                    |                     |      |                    |                            |             |
| Unadjusted                   |                    |                            |             |                    |                     |      |                    |                            |             |
| BMI (per five unit increase) | 395                | 1.08 (0.93 to 1.26)        | 0.30        | 144                | 1.06 (0.77 to 1.46) | 0.72 | 539                | 1.08 (0.94 to 1.24)        | 0.28        |
| Adjusted*                    |                    |                            |             |                    |                     |      |                    |                            |             |
| BMI (per five unit increase) | 395                | <b>1.24 (1.05 to 1.47)</b> | 0.01        | 144                | 1.09 (0.79 to 1.52) | 0.59 | 539                | <b>1.21 (1.04 to 1.40)</b> | <b>0.01</b> |
| BMI categorical              |                    |                            |             |                    |                     |      |                    |                            |             |
| Unadjusted                   |                    |                            |             |                    |                     |      |                    |                            |             |
| BMI <25                      | 107                | ref                        |             | 31                 | ref                 |      | 138                | ref                        |             |
| 25–30                        | 138                | 1.08 (0.68 to 1.73)        | 0.74        | 53                 | 2.64 (0.94 to 7.40) | 0.07 | 191                | 1.26 (0.82 to 1.93)        | 0.29        |
| >=30                         | 150                | 1.17 (0.74 to 1.85)        | 0.50        | 60                 | 1.53 (0.53 to 4.38) | 0.43 | 210                | 1.22 (0.80 to 1.86)        | 0.35        |
| Adjusted*                    |                    |                            |             |                    |                     |      |                    |                            |             |
| BMI <25                      | 107                | ref                        |             | 31                 | ref                 |      | 138                | ref                        |             |
| 25–30                        | 138                | 1.37 (0.83 to 2.25)        | 0.22        | 53                 | 2.88 (0.97 to 8.60) | 0.06 | 191                | 1.55 (0.99 to 2.45)        | 0.06        |
| >=30                         | 150                | <b>1.78 (1.09 to 2.91)</b> | <b>0.02</b> | <b>60</b>          | 1.74 (0.58 to 5.23) | 0.32 | 210                | <b>1.78 (1.13 to 2.78)</b> | <b>0.01</b> |

\*Adjusted for age and sex.  
MOON, Multicenter Orthopaedic Outcomes Network; ROW, Rotator Cuff Outcomes Workgroup.

BMI in patients with rotator cuff pathology could mitigate muscle loss and even potentially help to rebuild lost muscle mass.

One potential mechanism through which obesity might influence muscle atrophy in the setting of rotator cuff tear is through the inflammatory pathway. Obesity is well known to promote chronic low grade, proinflammatory state through the systemic recruitment and activation of proinflammatory cytokines, such as tumour necrosis factor  $\alpha$  and interleukin-6, from white adipose tissue.<sup>39–42</sup> These proinflammatory cytokines not only inhibit insulin action in metabolic tissues but also influence cell growth and apoptosis.<sup>43</sup> In the setting of rotator cuff injury, these proinflammatory cytokines have been shown to activate nuclear factor kappa B (NF- $\kappa$ B),<sup>44</sup> inducing apoptosis in musculotendinous units and therefore promoting muscle atrophy.<sup>45–49</sup> Furthermore, chronic low-grade NF- $\kappa$ B activation as in the setting of obesity inhibits the regeneration pathway, further perpetuating the atrophic state.<sup>45–49</sup> Therefore, given the well-established links between muscle atrophy and adverse surgical outcomes,<sup>7–13</sup> obesity could provide a modifiable risk factor for muscle atrophy, potentially yielding improvements in clinical outcomes and enhancing eligibility for surgical interventions.

Ultimately, our study shows a positive association between BMI and muscle atrophy among patients with rotator cuff tear. Given the importance of muscle atrophy in determining the outcome and selection of treatments in patients with rotator cuff tears, our study serves as a steppingstone for future causal studies in the field. This work, in combination with existing data, emphasises the need and potential benefit of future research into the potential modification or targeting of obesity (for example with glucagon-like peptide-1 agonists like Ozempic) early in patients with rotator cuff tears to improve success rates of rotator cuff surgeries and quality of life through reduction or even reversal of muscle atrophy.

## LIMITATIONS

There are two main limitations of this study. First, the utilisation of two cohorts in our study design led to differences in patient and tear characteristic assessment. Namely, we were unable to assess clinical factors (such as steroid injection or medical comorbidities) or social factors (such as physical activity, occupation, nutrition, etc) as this data was not consistently collected in both cohorts. Though for the most part, this limitation would not be expected to influence the overall findings of the study as these unavailable factors would contribute only to sensitivity analyses, it is possible that physical activity might influence both muscle atrophy and BMI and thus serve as a confounder. However, even in this scenario, although obesity may not be a causal factor, it could serve as an easily identifiable predictive factor for muscle atrophy in individuals with cuff tears. Overall, while the dual cohort study increases generalisability and

confidence of these findings, further investigation into the role of physical activity is needed.

Second, the cross-sectional nature of our study limits our ability to establish causality definitively. While our findings suggest that higher BMI is associated with increased muscle atrophy, we acknowledge the inherent limitation of all observational studies is an inability to establish causality. Namely, cross-sectional studies, such as these, are limited in their ability to infer temporality (ie, we do not know if patients were obese prior to developing muscle atrophy) and are thus at risk of reverse causality and unable to evaluate for evidence of causal relationships. Therefore, further investigations, for example, a prospective cohort study, to elucidate temporality and/or potential causal associations and their implications are warranted and a useful next step.

## CONCLUSIONS

Higher BMI was associated with significantly higher odds of muscle atrophy in RCT patients. More study is needed to understand why and how this relationship exists, as well as whether interventions to reduce BMI may help improve outcomes for these patients.

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