Body composition and knee cartilage properties in healthy, community-based adults

Yuanyuan Wang, Anita E Wluka, Dallas R English, Andrew J Teichtahl, Graham G Giles, Richard O’Sullivan, Flavia M Cicuttini

Background: Although obesity is widely accepted as a risk factor for knee osteoarthritis, whether weight per se or the specific components of body composition are the major determinants of properties of articular knee cartilage is unclear.

Objective: To examine associations between anthropometric and body composition measures and knee cartilage properties in healthy adults.

Methods: 297 healthy adults with no clinical knee osteoarthritis were recruited from an existing community-based cohort. Anthropometric measures and body composition, including fat-free mass and fat mass assessed using bioelectrical impedance analysis, were measured at baseline (1990–4) and current follow-up (2003–4). Tibial cartilage volume and tibiofemoral cartilage defects were assessed using MRI at follow-up.

Results: After adjustment for potential confounders, baseline and current fat-free mass, independent of fat mass, were positively associated with tibial cartilage volume (all p<0.001). Increased fat-free mass over the time period was positively associated with tibial cartilage volume (p<0.001). Current fat mass was negatively associated with tibial cartilage volume (p=0.004). Baseline and current fat mass were weakly associated with increased tibiofemoral cartilage defects (p=0.06 and p=0.07, respectively), independent of fat-free mass.

Conclusion: The findings suggest a beneficial effect of fat-free mass, but a deleterious effect of fat mass, on knee cartilage properties in healthy adults. This suggests that weight-loss programmes aimed at reducing fat mass but maintaining muscle mass may be important in preventing the onset and/or progression of knee osteoarthritis.
our inclusion criteria and had attended the first year of round 3 follow-up of the MCCS, which started in 2003. We used quota sampling whereby recruitment ceased when our target sample of about 300 subjects was achieved. The study was approved by The Cancer Council Victoria Human Research Ethics Committee and the Standing Committee on Ethics in Research Involving Humans of Monash University. All participants gave written informed consent.

**Anthropometric measures**

At the MCCS baseline (1990–4), height, weight, waist and hip circumferences were measured using standardised written protocols. Baseline BMI (weight/height\(^2\), kg/m\(^2\)) and WHR were calculated from these data. Weight was measured using electronic scales with bulky clothing removed at the current follow-up (2003–4). Current BMI was calculated.

Bioelectrical impedance analysis was performed with a single-frequency (50 kHz) electric current produced by a BIA-101A RJL system analyser (RJL systems, Detroit, Michigan, USA), at baseline and current follow-up. Resistance and reactance were measured with subjects in the supine position. We used bioimpedance analysis to estimate non-adipose mass, hereafter termed fat-free mass (FFM, as \(9.1356 + (0.4273 \times \text{height}^2/\text{resistance}) + (0.0667 \times \text{reactance})\)) for men, and \(7.7435 + (0.4542 \times \text{height}^2/\text{resistance}) + (0.119 \times \text{weight} + (0.0455 \times \text{reactance})\)) for women. Adipose mass, hereafter termed fat mass (FM; weight − FFM) and percentage of fat (FM divided by weight) were subsequently calculated.

**MRI and the measurement of cartilage volume and cartilage defects at current follow-up**

At the current follow-up during 2003–4, each subject had an MRI performed on the dominant knee (defined as the leg used to step-off from when walking was initiated). Knees were imaged on a 1.5 T whole-body magnetic resonance unit (Philips Netherlands) using a commercial transmit–receive extremity MRI unit. The knee was imaged using a sagittal T\(_1\)-weighted sequence, with a slice thickness of 3 mm, using the following sequence parameters: TR 4000 ms, TE 16 ms, matrix 256 × 160, and a field of view of 18 cm. This gave a spatial resolution of 1.4 × 1.4 × 3 mm\(^3\). Tibial cartilage volume was determined by image processing using Osiris software (Geneva, Switzerland) as previously described. The coefficients of variation for cartilage volume measurements were 2.1% for medial tibial and 2.2% for lateral tibial cartilage.

Cartilage defects were graded on the MR images with a classification system as previously described for the medial and lateral tibial and femoral cartilages. A cartilage defect was identified as present if there was irregularity on the cartilage surface or bottom with loss of cartilage thickness on at least two consecutive slices. Intrarater and interobserver reliability assessed in 50 MR images (expressed as intraclass correlation coefficient) were 0.90 and 0.90 for the medial tibiofemoral compartment and 0.89 and 0.85 for the lateral tibiofemoral compartment, respectively. Tibial plateau cross-sectional area was used as a measure of tibial bone size. It was directly measured using images reformatted in the axial plane using Osiris software as previously described. Coefficients of variation for the medial and lateral tibial plateau areas were 2.3% and 2.4%, respectively.

**Statistical analysis**

Outcomes were tibial cartilage volume and the presence of tibiofemoral cartilage defects assessed at current follow-up. Tibial cartilage volume was assessed for normality, thus linear regression was used. The presence/absence of cartilage defects was a dichotomous outcome, thus logistic regression was used. Multiple regression models were constructed to explore the relationship between anthropometric and body composition measures and knee cartilage properties, with adjustment for the potential confounders of age, gender and tibial plateau bone area (for tibial cartilage volume only). In terms of anthropometric and body composition measures, we analysed baseline variables, current follow-up variables, and the change in these variables (current follow-up values – baseline values) separately. To further examine body mass distribution as a predictor of the different knee cartilage features, we fitted FFM and FM simultaneously as continuous variables in the same model. p < 0.05 were considered to be significant. All analyses were performed using the SPSS statistical package (standard version 14.0; SPSS, Chicago, Illinois, USA).

**RESULTS**

Table 1 presents the characteristics of the 297 participants (age range 50–79 years (mean (SD) 58.0 (5.5) years). Cartilage defects were more common in women (124 (66.7%) compared with 60 (54.1%) in men). There were no significant differences between this population and the original MCCS population, which has the following profile: 61% women, mean (SD) age 57.8 (3.0) years and BMI 25.7 (3.8) kg/m\(^2\). There were no significant differences in dietary intake or other health-related behaviours (data not shown). There were current body

<table>
<thead>
<tr>
<th>Table 1 Characteristics of study subjects (n = 297) at baseline (1990–4) and follow-up (2003–4)</th>
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</thead>
<tbody>
<tr>
<td><strong>At baseline</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Height (cm)</td>
</tr>
<tr>
<td>Weight (kg)</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
</tr>
<tr>
<td>Hip circumference (cm)</td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
</tr>
<tr>
<td>Tibial cartilage volume (mm(^3))</td>
</tr>
<tr>
<td>Tibial plateau bone area (mm(^2))</td>
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<tr>
<td>Presence of cartilage defects</td>
</tr>
</tbody>
</table>

*Difference in variables between baseline and current follow-up, using paired-samples t test.
†Data available on 294 subjects.
‡Data available on 233 subjects.

Except where indicated, values are mean (SD).
composition measures for 233 (78.5%) subjects. This group had lower baseline weight (p = 0.05) and BMI (p = 0.01) than those without current body composition measures. There were no significant differences in terms of baseline height (p = 0.87), FFM (p = 0.06) and FM (p = 0.41) between the two groups. There were significant increases in body weight, BMI and FM associated with tibial cartilage volume (p = 0.05) in multivariate analyses. After adjustment for FFM and FM, FFM was positively associated with tibial cartilage volume (p = 0.001), and body weight was weakly positively associated with tibial cartilage volume (p = 0.05). Weight was negatively associated with tibial cartilage volume. In multivariate analyses adjusted for age, gender and tibial plateau bone area, only FFM remained positively associated with tibial cartilage volume (p<0.001). After adjustment for FFM and FM, FFM was positively associated with tibial cartilage volume (p<0.001). Fat mass was weakly negatively associated with tibial cartilage volume (p = 0.08). WHR was not significantly associated with tibial cartilage volume (p = 0.59).

Similar results were found when current anthropometric and body composition measures were examined (table 2). Current FFM was positively associated with tibial cartilage volume (p<0.001), and body weight was weakly positively associated with tibial cartilage volume (p = 0.05) in multivariate analyses. After adjustment for FFM and FM, FFM was positively associated with tibial cartilage volume (p = 0.001) in multivariate analyses adjusted for age and gender. FFM and FM were positively associated with tibial cartilage volume. Percentage of fat was negatively associated with tibial cartilage volume. In multivariate analyses adjusted for age, gender and tibial plateau bone area, only FFM remained positively associated with tibial cartilage volume (p<0.001). After adjustment for FFM and FM, FFM was positively associated with tibial cartilage volume (p<0.001). Fat mass was weakly negatively associated with tibial cartilage volume (p = 0.08). WHR was not significantly associated with tibial cartilage volume (p = 0.59).

### Relationship between anthropometric and body composition measures and tibial cartilage volume

The associations between baseline anthropometric and body composition measures and current tibial cartilage volume were examined (table 1). In univariate analyses, body weight, BMI, waist circumference, WHR and FFM were all positively associated with tibial cartilage volume. Percentage of fat was negatively associated with tibial cartilage volume. In multivariate analyses adjusted for age and gender and tibial plateau bone area, respective baseline variable in the regression equation.

<table>
<thead>
<tr>
<th>Variables at baseline (1990–4)</th>
<th>Univariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>1.01 (0.99 to 1.03)</td>
<td>0.25</td>
<td>1.03 (1.01 to 1.06)</td>
<td>0.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>1.07 (1.00 to 1.14)</td>
<td>0.05</td>
<td>1.09 (1.01 to 1.16)</td>
<td>0.02</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>1.01 (0.99 to 1.03)</td>
<td>0.28</td>
<td>1.04 (1.01 to 1.06)</td>
<td>0.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>0.99 (0.96 to 1.01)</td>
<td>0.30</td>
<td>1.06 (1.00 to 1.12)</td>
<td>0.04</td>
<td>1.03 (0.97 to 1.10)</td>
<td>0.34</td>
</tr>
<tr>
<td>Percentage of fat (%)</td>
<td>1.05 (1.02 to 1.08)</td>
<td>0.003</td>
<td>1.04 (1.01 to 1.08)</td>
<td>0.01</td>
<td>1.04 (1.00 to 1.07)</td>
<td>0.06</td>
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</table>

<table>
<thead>
<tr>
<th>Variables at current follow-up (2003–4)</th>
<th>Univariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>1.01 (0.99 to 1.03)</td>
<td>0.22</td>
<td>1.03 (1.01 to 1.05)</td>
<td>0.01</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>1.06 (1.00 to 1.12)</td>
<td>0.05</td>
<td>1.07 (1.01 to 1.14)</td>
<td>0.03</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fat-free mass (kg)</td>
<td>0.99 (0.96 to 1.01)</td>
<td>0.25</td>
<td>1.07 (1.01 to 1.13)</td>
<td>0.03</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>1.05 (1.02 to 1.09)</td>
<td>0.004</td>
<td>1.05 (1.01 to 1.08)</td>
<td>0.01</td>
<td>1.04 (1.00 to 1.09)</td>
<td>0.07</td>
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</table>

<table>
<thead>
<tr>
<th>Change in the following variables</th>
<th>Univariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
<th>Multivariate analysis (odds ratio (95%CI))</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>1.01 (0.97 to 1.06)</td>
<td>0.61</td>
<td>1.01 (0.97 to 1.07)</td>
<td>0.57</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>1.03 (0.91 to 1.17)</td>
<td>0.63</td>
<td>1.04 (0.90 to 1.18)</td>
<td>0.62</td>
<td>–</td>
<td>–</td>
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<tr>
<td>Fat-free mass (kg)</td>
<td>1.01 (0.92 to 1.11)</td>
<td>0.82</td>
<td>1.04 (0.94 to 1.14)</td>
<td>0.47</td>
<td>0.98 (0.87 to 1.10)</td>
<td>0.71</td>
</tr>
<tr>
<td>Fat mass (kg)</td>
<td>1.04 (0.97 to 1.10)</td>
<td>0.27</td>
<td>1.04 (0.97 to 1.11)</td>
<td>0.25</td>
<td>1.03 (0.97 to 1.10)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

*Univariate analysis of cartilage defects per unit increase in the respective anthropometric and body composition measure after adjustment for age and gender in the regression equation.
†Odds ratio of cartilage defects per unit increase in the respective anthropometric and body composition measure after adjustment for fat-free mass and fat mass, ie, including age, gender, fat-free mass and fat mass in the regression equation.
‡Adjusted for age, gender and respective baseline variable in the regression equation.
associated with tibial cartilage volume \((p<0.001)\). FM was negatively associated with tibial cartilage volume \((p = 0.004)\).

Increase in FFM over the time period was positively associated with tibial cartilage volume in both univariate and multivariate analyses \((p = 0.03)\). This association persisted after adjustment for both FFM and FM \((p<0.001)\). Changes in body weight, BMI and FM were not significantly associated with tibial cartilage volume \((table 2)\).

**Relationship between anthropometric and body composition measures and the presence of tibiofemoral cartilage defects**

The associations between baseline anthropometric and body composition measures and the presence of current tibiofemoral cartilage defects were examined \((table 3)\). In univariate analyses, BMI, FM and percentage of fat were positively associated with the presence of tibiofemoral cartilage defects. In multivariate analyses adjusted for age and gender, body weight, BMI, waist circumference, WHR, FFM, FM and percentage of fat were all positively associated with the presence of tibiofemoral cartilage defects, with odds ratios ranging from 1.03 to 1.09 \((all \ p < 0.04)\). After adjustment for FFM and FM, FM was weakly positively associated with the presence of tibiofemoral cartilage defects \((p = 0.06)\). FFM \((p = 0.34)\) and WHR \((p = 0.21)\) were no longer significantly associated with the presence of tibiofemoral cartilage defects.

Similar results were obtained when current anthropometric and body composition measures were examined \((table 3)\). Current FM was weakly positively associated with the presence of tibiofemoral cartilage defects \((p = 0.07)\), but no effect of FFM \((p = 0.37)\), after adjustment for FFM and FM.

Changes in body weight, BMI, FFM and FM over the time period were not significantly associated with the presence of tibiofemoral cartilage defects, in both univariate and multivariate analyses \((table 3)\).

The results were similar when the above analyses were repeated for men and women separately \((data not shown)\).

**DISCUSSION**

In this population of healthy community-based adults with no clinical knee OA, baseline \((1990–4)\) and current \((2003–4)\) FFM were both positively associated with tibial cartilage volume, independent of FM. Increase in FFM over the time period was associated with an increase in tibial cartilage volume. In contrast, FM was associated with an adverse effect on knee cartilage. Current FM was associated with reduced tibial cartilage volume, and both baseline and current FM were associated with an increase in tibiofemoral cartilage defects, independent of FFM. Taken together, these findings suggest a beneficial effect of FFM, but a negative effect of FM, on knee cartilage in healthy people.

In this study, we found compelling evidence for a beneficial effect of FFM on cartilage. Both current FFM and FFM measured 10 years earlier were associated with an increased tibial cartilage volume in healthy people independent of FM. It has been shown that increased muscle size and mass is related to increased knee cartilage volume.\(^ {21} \) We have also recently shown that lower muscle mass is associated with an increased loss of medial and lateral tibial cartilage over 2 years in people without knee OA.\(^ {4} \) In the present study, we also showed an additional beneficial effect of increase in FFM over time that was associated with increased cartilage volume. These data suggest that increased muscle mass, including gains later in life, may be protective against the loss of cartilage volume. The mechanism by which this occurs is not known but may be due to greater stabilisation at the knee joint during dynamic tasks. The effect of FFM on cartilage volume cannot simply be explained by physical activity, because adjustment for physical activity in the analyses did not change our findings \((results not shown)\). Although it may be that muscle mass and cartilage volume are co-inherited, our finding that an increase in FFM over the time period was associated with increased tibial cartilage suggests that muscle mass is an important determinant of cartilage volume. These data suggest that a change in muscle mass has the capacity to affect changes in cartilage volume.

Obesity is an established risk factor for cardiovascular disease as well as knee OA.\(^ {1, 2} \) However, unlike for cardiovascular disease,\(^ {4} \) the distribution of body fat has been inconsistently associated with the risk of knee OA.\(^ {2, 4} \) A recent cross-sectional study showed that BMI, FM, percentage FM and waist circumference were higher in women with OA than in those without, but that there were no differences in WHR between the two groups.\(^ {22} \) We found that BMI was associated with an increased presence of cartilage defects, which is consistent with a previous study showing a correlation between BMI and an increased prevalence and severity of cartilage defects.\(^ {23} \) Although BMI is a good measure of body weight, independent of height, it fails to distinguish between adipose and non-adipose body mass.\(^ {2} \) Our data suggest a negative effect of FM on knee cartilage, with a reduction in volume and an increase in cartilage defects. Moreover, the positive association between FFM and WHR and knee cartilage defects found in this study could be explained by the effect of FM. Cartilage defects have previously been shown to be predictive of cartilage loss, independent of cartilage volume, suggesting a continuum from normal to abnormal cartilage even in healthy people, and that the defects may represent early cartilage abnormalities.\(^ {24} \) It is therefore possible that FM may be an important factor in the development and progression of cartilage defects, ultimately leading to longitudinal cartilage loss and knee OA. This may be important in helping to understand the association between obesity and the onset and/or progression of OA.

A potential limitation of this study was the method used to assess body composition. Body composition can be estimated by several different techniques. For instance, lean body mass can be considered a surrogate measure of muscle mass.\(^ {25} \) In this study, we used FFM, which is the total weight of the body without any fat, referring to all skeletal bones and muscles and other body tissues not containing fat, as a surrogate measure of muscle mass. However, FFM may not always accurately reflect specific changes in muscle mass or differences in muscle mass between individuals.\(^ {26} \) Nevertheless, our findings persisted after adjustment for age, gender and bone size \(\text{tibial plateau bone area}\), confirming that FFM was a more accurate measure of muscle mass.

A potential strength of our study is that we examined both current body composition as well as data objectively collected about 10 years earlier. This has been recently raised in the context of examining risk factors for OA, particularly in relation to obesity, as any development of symptomatic disease may be associated with a reduction in physical activity and obesity.\(^ {27} \) In this study we examined asymptomatic people and used a novel methodology that allowed us to examine knee cartilage in a sensitive, validated way. This allowed us, for the first time, to examine cartilage in a continuum from the healthy through to the diseased state so that we can examine the effect of body composition on knee joint morphology in asymptomatic people with no disease or early subclinical disease.

How FFM confers a beneficial effect on knee cartilage whereas FM is associated with a reduction in cartilage and an increase in defects is unclear. The emerging data suggest that beneficial effects of FFM on the joint may be related to biomechanical stabilisation of the joint.\(^ {27} \) Obesity increases

### references

1. [Link to reference 1](http://example.com)
2. [Link to reference 2](http://example.com)
3. [Link to reference 3](http://example.com)
4. [Link to reference 4](http://example.com)
5. [Link to reference 5](http://example.com)
6. [Link to reference 6](http://example.com)
7. [Link to reference 7](http://example.com)
joint loading, which may predate cartilage degeneration at weight-bearing sites such as the knee. However, if this were the only explanation, we would expect a similar effect of FFM, which was not the case. Furthermore, our findings that WHR was not associated with an increased presence of tibiofemoral cartilage defects, independent of FM, suggest that this pattern of fat distribution may not be important in OA. However, it has long been recognised that the effect of obesity cannot simply be explained by the biomechanical effect of weight. For example, it has previously been suggested that OA at non-weight-bearing sites such as the carpometacarpal joints and the proximal interphalangeal joints of the hands may be due to metabolic factors related to adiposity. It may be that hormones such as leptin that indirectly reflect body fat stores and have a role in immunomodulation may be important in OA. Chondrocytes from joint cartilage have been shown to express leptin receptors, which, when stimulated, produce nitric oxide, leading to inflammatory alterations in cartilage including phenotype loss of chondrocytes, apoptosis and metalloproteinase activation.

In this population of healthy adults, our results suggest a beneficial effect of baseline FFM, current FFM and increase in FFM on tibial cartilage volume over the time period of the study. In contrast, FM was deleterious, being associated with a reduction in tibial cartilage volume and an increase in tibiofemoral cartilage defects independent of FFM. The relative importance of these factors differed according to structure, possibly suggesting different mechanisms of effect. These data suggest that weight-loss programmes aimed at reducing FM but preserving/increasing FFM may be important in maintaining cartilage health, thus preventing the onset and/or progression of knee OA.

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Competing interests: None.

REFERENCES