Cartilage defects are associated with physical disability in obese adults

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Objective. To describe the associations between physical disability measures and knee cartilage defects in obese adults.

Methods. One hundred and eleven obese subjects were recruited from laparoscopic adjustable gastric banding or exercise/diet weight loss programmes. All subjects completed disease-specific (WOMAC) and general health status (SF-36) questionnaires, and were assessed for range of knee motion, tibiofemoral alignment and quadriceps strength. Knee cartilage defects were graded on MRI according to established protocol. Regression analysis was adjusted for age, gender, BMI and presence of clinical knee OA.

Results. The association between higher whole compartment cartilage defect scores and increasing BMI, age and clinical knee OA was confirmed in this obese cohort \((r=0.27, P=0.01; r=0.26, P=0.007; P<0.0001,\) respectively), whereas new associations were found with reduced knee range of motion \((r=0.5, P<0.0001)\). No associations were found between defect scores and quadriceps strength. Varus malalignment was associated with higher medial cartilage defect scores \((r=0.33, P=0.013)\). Higher levels of pain, stiffness and physical disability (WOMAC, SF-36) were associated with higher medial compartment and patella cartilage defect scores.

Conclusions. Knee cartilage defects increase with increasing obesity and are associated with both objective and self-reported measures of physical disability. Longitudinal studies are required to assess the potential for change or improvement in cartilage defects with weight loss.

Key words: Cartilage defects, MRI, Obesity, Clinical osteoarthritis, Range of motion, Alignment, Quadriceps strength.

Introduction

OA is a chronic disease characterized by gradual degradation of cartilage and failure of supporting joint tissues. Large longitudinal studies have demonstrated that obesity is a significant risk factor for both the incidence and progression of tibiofemoral knee OA (both symptomatic and radiographic disease) [1–3].

MRI allows the direct visualization of articular cartilage defects, is highly reproducible and correlates with histological and arthroscopic findings [4]. Cartilage defects are significantly associated with disease severity in OA, and predict knee cartilage loss and knee replacement surgery [5]. Obesity has been associated with increased knee cartilage defect severity and prevalence in tibiofemoral and patellar compartments, particularly in women [5–8].

However, despite the increased societal burden consequent to the global obesity epidemic, there is little information about the clinical implications of cartilage defects in obese people. The aim of this cross-sectional study of obese adults was to evaluate the associations between knee cartilage defects and both objective and self-reported measures of physical disability.

Patients and methods

Subjects

This study was carried out in Northern Sydney between 2006 and 2008. Ethics approval for the study was obtained from the Northern Sydney Central Coast Area Health Service Human Research Ethics Committee and the University of Sydney, and informed consent was obtained from all the study participants.

Subjects were recruited and assessed at the commencement of surgical (laparoscopic-adjustable gastric banding) and non-surgical (diet and exercise) weight loss programmes. All subjects were obese, most belonging to obesity Grade 2 or higher (obesity Grade 1: 30 ≤ BMI < 35; Grade 2: 35 ≤ BMI < 40; Grade 3: BMI ≥ 40). Apart from the usual MRI exclusion criteria, clinical exclusion criteria included inflammatory arthritis or psychiatric illness.

Physical disability assessment

Consenting study participants underwent physical assessment by a rheumatologist, including knee joint line tenderness, patellofemoral crepitus, bony enlargement, warmth, knee range of motion, tibiofemoral alignment [9] and quadriceps muscle strength [10]. Knee range of motion was assessed using a long-arm goniometer (total range between full flexion and extension) [11]. Tibiofemoral alignment was assessed using a goniometer (varus being negative, neutral being 0 and valgus being positive) [12]. Isometric quadriceps strength (mean of three readings) was assessed using a hand-held dynamometer (Stamina, Germany). Knee pain, physical function and general health status were self-reported using the WOMAC [13] and Medical Outcomes Study Short Form 36 questionnaire (SF-36) [14].

The ACR clinical classification criteria were used to define knee OA [15].

Cartilage defect assessment

Eligible subjects underwent baseline MRI of the symptomatic or dominant asymptomatic knee. Sagittal MRI images were obtained on a 3T scanner (Magnetom Trio; Siemens, Erlangen, Germany) with a transmit/receive knee extremity coil (T1-weighted fat saturation 3D FISP; flip angle 20°; repetition time 31 ms; echo time 9.53 ms; field of view 160 mm; 60 partitions; 512 × 384 matrix; acquisition time 15 min; one acquisition, slice thickness 1.5 mm). Cartilage defects were assessed by a single trained reader (A.A.) blinded to clinical and laboratory results. Cartilage defects (score range 0–4) were graded at median
tibiofemoral, lateral tibiofemoral and patellar sites as previously described [16]. A cartilage defect had to be present in at least two consecutive sections. Cartilage defect scores for medial tibiofemoral (range 0–8), lateral tibiofemoral (range 0–8), patellar (range 0–4) and whole (composite, range 0–20) compartments were computed. A prevalent cartilage defect was defined as a score of ≥2 at any site within that compartment. Intra-observer reliability was measured using intra-class coefficients after repeat mapping 1 week apart for 20 subjects (intra-class correlation coefficients were 0.98 for medial tibiofemoral, 0.98 for lateral tibiofemoral and 1.00 for patella).

Pearson’s correlation analysis was used to analyse the association between cartilage defects (in each compartment) and age, gender and BMI. The Mann–Whitney U-test was used to assess the relationship between cartilage defects and the presence of clinical knee OA. The Kruskal–Wallis test was used to assess differences in joint pain, physical performance and self-report measures according to BMI grade. Linear regression was used to examine associations between collected clinical variables, self-report measures and cartilage defect scores. Multiple linear regression analysis adjusted for age, gender, BMI and presence of clinical knee OA. A P-value <0.05 (two tailed) was considered to demonstrate statistical significance (SPSS statistical package, standard version 14.0; SPSS, Chicago, IL, USA).

### Results

A total of 333 (221 non-surgical and 112 surgical) subjects were screened and 163 (50%) agreed to participate. One hundred and eleven subjects underwent a MRI scan (45 did not meet MRI criteria, 7 withdrew prior to MRI).

The main demographic characteristics of the study cohort are presented in Table 1. Nineteen (17%) subjects had Grade 1 obesity, 40 (36%) Grade 2 and 52 (47%) Grade 3. The mean WOMAC scores indicated a high level of joint pain and physical disability. The proportion of prevalent cartilage defects at the medial tibiofemoral, lateral tibiofemoral and patella sites were 57, 55 and 43%, respectively.

Age and the presence of clinical knee OA were significantly positively associated with cartilage defect scores in each compartment, except the lateral tibiofemoral. There were no significant gender differences in cartilage defect scores.

In univariate regression analysis, there was a significant positive correlation between BMI and cartilage defect scores in each compartment, except the lateral tibiofemoral site (medial tibiofemoral: \( r = 0.21, P = 0.028 \); patella: \( r = 0.21, P = 0.026 \); whole joint: \( r = 0.26, P = 0.007 \)). Increasing grades of obesity were associated with more severe cartilage defect scores in the lateral \( (P = 0.027) \), patella \( (P = 0.041) \) and whole \( (P = 0.019) \) compartments.

### Objective physical measures

Knee range of motion was significantly associated with cartilage defect scores in all compartments in univariate analysis (whole compartment: \( r = -0.504, P < 0.0001 \)). The observations remained significant in multivariate analysis after adjustment for age, gender, BMI and knee OA (Table 2; \( r^2 = 0.26, P = 0.001 \)). Varus knee alignment was associated with medial compartment cartilage defect scores \( (r = 0.33, P = 0.013) \). A trend for significance remained in multivariate analysis \( (r^2 = 0.236, P = 0.07) \) (Table 2). However, valgus knee alignment was not associated with cartilage defect scores. Men had significantly higher quadriceps strength than women \( (P < 0.0001) \). No association was found between quadriceps strength and cartilage defect scores, with and without adjustment for gender. The model that included knee range of motion, knee alignment and quadriceps strength adjusted for age, gender, BMI and knee OA accounted for 33% of the variance in whole cartilage defects \( (r^2 = 0.33, P < 0.0001) \).

### Self-reported measures (WOMAC and SF-36)

Poor WOMAC pain, stiffness and function scores were significantly associated with worse cartilage defect scores in medial tibiofemoral, patella and whole compartment (Table 2) in multivariate analysis. Subjects with worse cartilage defect scores in these compartments also had lower SF-36 physical component scores (physical function, role physical, bodily pain and general health subscales). After adjustment for confounders, the associations remained significant for physical function, bodily pain (medial, whole compartments) and general health (medial compartment) (Table 2). No associations were found between cartilage defect scores and SF-36 mental component scores. The multivariate model that included WOMAC pain, stiffness and function scores adjusted for age, gender, BMI and knee OA

### Table 1. Characteristics of the cohort (n = 111)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean ± S.D.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>51 ± 11.6</td>
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<tr>
<td>Female, %</td>
<td>70</td>
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<tr>
<td>BMI, kg/m²</td>
<td>39.9 ± 5.8</td>
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<tr>
<td>Surgery for weight loss, %</td>
<td>42</td>
</tr>
<tr>
<td>Clinical knee OA, %</td>
<td>34</td>
</tr>
<tr>
<td>Knee range of motion, °</td>
<td>115 ± 10</td>
</tr>
<tr>
<td>Varus knee alignment, %</td>
<td>69</td>
</tr>
<tr>
<td>Quadriceps strength, lb</td>
<td>52 ± 20</td>
</tr>
<tr>
<td>WOMAC pain (0–20)</td>
<td>7.8 ± 3.8</td>
</tr>
<tr>
<td>WOMAC stiffness (0–6)</td>
<td>3.7 ± 1.6</td>
</tr>
<tr>
<td>WOMAC function (0–68)</td>
<td>26.1 ± 12.5</td>
</tr>
<tr>
<td>SF physical function (0–100)</td>
<td>62.8 ± 26.9</td>
</tr>
<tr>
<td>SF role physical (0–100)</td>
<td>58.8 ± 43.9</td>
</tr>
<tr>
<td>SF bodily pain (0–100)</td>
<td>54.7 ± 23.8</td>
</tr>
<tr>
<td>SF general health (0–100)</td>
<td>57.0 ± 21.5</td>
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</table>

### Table 2. Associations between cartilage defect scores, physical measures and quality of life variables

<table>
<thead>
<tr>
<th></th>
<th>Medial TF</th>
<th>Lateral TF</th>
<th>Patella</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td><strong>Physical measures</strong></td>
<td></td>
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<tr>
<td>Knee range of motion</td>
<td>-0.067 (-0.104, -0.029)</td>
<td>-0.031 (-0.058, -0.004)</td>
<td>-0.030 (-0.055, -0.004)</td>
<td>-0.124 (-0.187, -0.061)</td>
</tr>
<tr>
<td>Varus knee alignment</td>
<td>-0.345 (-0.720, 0.030)</td>
<td>NA</td>
<td>-0.014 (-0.257, 0.228)</td>
<td>-0.365 (-0.970, 0.240)</td>
</tr>
<tr>
<td>Valgus knee alignment</td>
<td>NA</td>
<td>0.080 (-0.157, 0.317)</td>
<td>-0.070 (-0.275, 0.136)</td>
<td>-0.072 (-0.455, 0.599)</td>
</tr>
<tr>
<td>Quadriceps strength</td>
<td>0.011 (-0.034, 0.012)</td>
<td>-0.008 (-0.025, 0.008)</td>
<td>0.002 (-0.013, 0.017)</td>
<td>-0.018 (-0.057, 0.020)</td>
</tr>
<tr>
<td><strong>Quality of life measures</strong></td>
<td></td>
<td></td>
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<tr>
<td>WOMAC pain</td>
<td>0.145 (0.051, 0.240)</td>
<td>0.011 (-0.057, 0.079)</td>
<td>0.075 (0.011, 0.139)</td>
<td>0.231 (0.070, 0.393)</td>
</tr>
<tr>
<td>WOMAC stiffness</td>
<td>0.306 (0.090, 0.523)</td>
<td>0.066 (-0.090, 0.221)</td>
<td>0.140 (-0.008, 0.287)</td>
<td>0.512 (0.143, 0.881)</td>
</tr>
<tr>
<td>WOMAC function</td>
<td>0.047 (0.017, 0.077)</td>
<td>0.010 (-0.012, 0.032)</td>
<td>0.026 (0.006, 0.046)</td>
<td>0.083 (0.032, 0.134)</td>
</tr>
<tr>
<td>SF physical function</td>
<td>-0.018 (-0.031, -0.004)</td>
<td>-0.002 (-0.012, 0.008)</td>
<td>-0.010 (-0.019, -0.001)</td>
<td>-0.029 (-0.053, -0.006)</td>
</tr>
<tr>
<td>SF role physical</td>
<td>-0.003 (-0.011, 0.005)</td>
<td>-0.002 (-0.007, 0.004)</td>
<td>-0.003 (-0.008, 0.002)</td>
<td>-0.008 (-0.021, 0.006)</td>
</tr>
<tr>
<td>SF bodily pain</td>
<td>-0.018 (-0.033, -0.003)</td>
<td>-0.003 (-0.014, 0.007)</td>
<td>-0.009 (-0.019, 0.001)</td>
<td>-0.030 (-0.056, -0.005)</td>
</tr>
<tr>
<td>SF general health</td>
<td>-0.020 (-0.037, -0.004)</td>
<td>0.002 (-0.009, 0.014)</td>
<td>-0.004 (-0.015, 0.007)</td>
<td>-0.023 (-0.050, 0.005)</td>
</tr>
</tbody>
</table>

Multivariate analysis (B: confidence limits). Data in bold denote statistically significant results \( (P < 0.05) \). *Adjusted for age, gender, BMI and clinical knee OA. TF: tibiofemoral.
accounted for 30% \( (r^2 = 0.30, P < 0.0001) \) of the variance in total cartilage defect scores.

**Discussion**

This cross-sectional study of 111 obese adults with and without symptomatic knee OA demonstrates importantly that knee cartilage defects in obese adults are associated with physical disability and reduced knee range of motion, even after accounting for the presence of clinical knee OA. These findings have not been described previously.

There was a high prevalence of clinical knee OA (34%) in this unselected mostly middle-aged obese cohort, confirming the high risk in this group. Further, the presence of clinical knee OA was positively associated with cartilage defect scores. We found a positive correlation for both BMI and age with cartilage defect scores as previously described [5, 6, 17]. Importantly, cartilage defect severity increased with increasing levels of obesity, and this has not been described previously.

We observed important associations between reduced range of knee movement and cartilage defect scores. The range of knee flexion and extension was lower in those with worse cartilage defect scores, and this remained significant after adjustment for age, gender, BMI and clinical knee OA. Cartilage integrity is dependent on cyclical loading [18–21]. Reduced knee range of motion in obese adults may result in increased vulnerability to injury in these areas of non-utilized cartilage, resulting in the development of cartilage defects. We hypothesize that weight loss and loss of subcutaneous fat may lead to a subsequent improvement in knee range of motion, particularly knee flexion. This may lead to improved cartilage nutrition resulting in a protective effect on cartilage, and ultimately reduced incidence and progression of cartilage defects. There has been contention regarding the mechanism of obesity-associated OA, i.e. metabolic and/or mechanical causes. Leptin and other adipocytokines have been postulated to be relevant in obesity-mediated OA [22]. These issues can be determined with longitudinal weight loss studies assessing knee cartilage structure, physical measures and adipocytokines. Longitudinal studies can also determine whether simple range of motion exercises may preserve cartilage integrity and prevent cartilage defects.

Varus knee alignment was associated with more severe medial cartilage defects scores, trending to significance after adjustment. A similar association was not found for valgus knee alignment, possibly due to the smaller representation in this cohort. An association between malalignment and knee cartilage defects has been described previously [4]. Interestingly, quadriceps strength was not associated with cartilage defect scores. This finding may partly be due to a floor effect with low quadriceps strength in the overall cohort.

Knee pain (WOMAC) was associated with cartilage defect scores in all compartments, except the lateral tibiofemoral, in multivariate analysis. Knee pain has been shown to correlate with chondral defects in other MRI studies using different definitions of knee pain [4]. This finding is interesting as hyaline articular cartilage does not contain nociceptive fibres. As the mechanism for the observed association with pain remains unclear, possibilities include mediation via substance P nociceptive fibres, super-induction of cyclooxygenase 2 and prostaglandins or other knee structural changes such as meniscal tears, synovitis or increased load transmission to bone [4]. Subchondral bone is recognized to be important in terms of pain and progression in OA [23]. Bone marrow lesions (BMLs) have been shown to be associated with knee pain in several studies [23]. BMLs are typically visualized on fat-suppressed T2-weighted or short T1 inversion recovery MRI images, and these sequences could not be incorporated into our study protocol due to image acquisition restrictions. The effect of BMLs on physical disability needs to be assessed in future studies.

We also observed the associations between cartilage defects and WOMAC stiffness and function. This has not been described before and indicates higher levels of disability in an already vulnerable population. Significant associations with cartilage defects were observed with SF-36 physical component scores. While a causal relationship cannot be established in cross-sectional analysis, it is pertinent that no associations were detected for non-physical or ‘mental component’ SF-36 measures. This suggests that cartilage defects may not reflect benign MRI findings and are associated not only with pain but also disability.

Cartilage defects have been implicated as important markers in the development and progression of knee OA, and are thought to reflect perhaps early change prior to loss of cartilage volume and subsequent radiographic change [4]. This is of particular relevance in obesity where the burden of chondral defects is increased. It would also be interesting to determine whether the association between knee cartilage defects and physical disability is similar for a non-obese sample. Nevertheless, it is important to note that our observations in this obese population held true regardless of co-existent clinical knee OA.

In conclusion, this is the first study, to our knowledge, to demonstrate associations of knee cartilage defects with objective physical measures such as knee range of motion, as well as self-reported pain, stiffness and physical function. We assessed an obese cohort, an at-risk population for incident and progressive knee OA. Improving knee range of motion through weight loss and exercise may help protect articular cartilage. Longitudinal studies are required to assess the potential for change or improvement in cartilage defects with weight loss.

**Rheumatology key messages**

- Cartilage defect severity is associated with reduced knee range of motion.
- Cartilage defect severity is associated with more knee pain, stiffness and physical disability.

**Acknowledgements**

We thank Elisia Manson, Metabolism & Obesity Services, RPAH, and Sarah Fisher, NS Private Hospital for help accessing patient records. We thank Peter Stanwell and Jeff McIntosh for performing the MR imaging; the Northern Clinical School, University of Sydney ARCHI (Advanced Research and Clinical High-field Imaging) for management of the 3T facility; and JS Chen, Rheumatology, RNSH, for statistical advice. We are also very grateful to the study participants.

**Funding:** This work was supported by a National Health and Medical Research Council Medical Postgraduate Research Scholarship (ID number 402901 to A.A.).

**Disclosure statement:** I.C. has spoken about obesity at meetings organized by Abbott Laboratories, Roche Products and Sanofi Aventis. All other authors have declared no conflicts of interest.

**References**