THE MECHANISM OF THE EFFECT OF OBESITY IN PATIENTS WITH KNEE OA: THE MEDIATING ROLE OF MALALIGNMENT

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Introduction. Obesity is a major risk factor for the development and progression of knee OA. Obesity is also linked to hip and possibly hand OA; at these sites, the association has been inconsistently detected and is weaker than at the knee. Ankle OA is rare and appears to have no relationship with obesity. Hypotheses to explain the obesity-OA relationship fall into metabolic and mechanical categories. The preponderance of studies has not revealed a metabolic link between obesity and OA. Less epidemiologic investigation has been devoted to exploring the mechanical hypothesis. The theory that the obesity-OA link reflects the effects of repetitive application of greater load does not explain why the obesity-associated odds of OA are so much higher at the knee than at the hip and ankle. This difference between lower extremity joint sites is consistent with the presence of a local factor (or factors) that intensifies the mechanical impact of excess body weight at the knee.

A key factor is the longer moment arm in reference to the center of gravity at the knee than at the hip or ankle. Alignment may be another important factor. Load distribution is more equitable in valgus than varus knees. In the newer ambulating knee, load is disproportionately transmitted to the medial compartment. Varus malalignment further increases medial load. However, with valgus malalignment, the medial compartment often continues to bear more load than the lateral compartment until severe valgus malalignment is present. Valgus knees may tolerate obesity better than varus knees. In theory, alignment is likely to influence the potency of obesity as a factor leading to knee OA—this has not been examined.

We hypothesized that: 1) the correlation between BMI and OA severity is weaker in valgus than in varus knees; and 2) that varus malalignment is an intervening factor in the causal chain between obesity and medialized osteoarthritis of the knee. If varus malalignment were playing this role, then body mass, the proximal factor, would correlate with varus malalignment, and the relationship between body mass and knee OA severity would be reduced after accounting for varus malalignment, the intervening factor.

Methods. 300 community-recruited patients with knee OA were enrolled into the baseline phase of an OA progression study. OA patients were required to have definite osteophytes in at least one knee, and at least "a little" difficulty with two or more tasks in the WOMAC physical function subscale. Exclusion criteria were: steroid injection within 3 months; any inflammatory arthritis; OA secondary to other diseases, e.g. Paget's, joint infection, chondrosis (see reference 1 for full list). IRB approval was obtained and all subjects provided informed consent.

To assess alignment, a single AP radiograph of the entire lower extremity was obtained using a 51 by 14 inch graduated grid cassette. The subject stood without footwear, positioned so that the tibial tubercles faced forward. The x-ray beam was centered at the knee at a distance of 8 feet. A setting of 100-300 milliampere-seconds and a kilovoltage of 80-90 was used depending on limb size and tissue characteristics to ensure landmark visualization. The alignment angle measured was formed by the intersection of the line from the center of the femoral head to the center of the femoral intercondylar notch, with the line from the center of the ankle talarus to the center of the tips of the tibial spines.

Knee x-rays were obtained in the same unit by 1 of 2 technicians. The radiographic protocol (2) addressed joint position, beam alignment, magnification, and landmark definition for measurements. The semi-flexed position was used, with fluoroscopic confirmation of joint position. Joint space was measured at the narrowest point for each compartment using electronic calipers. All radiographic measurements were made by a single experienced reader. Reliability was high for measurements of varus (ICC, model 1,1 0.99) and valgus (ICC 0.98) malalignment. The reliability for minimum joint space measurement [calculated from analyses of variance with repeated measures and ICCs (model 3,1)] was high for both medial and lateral compartments (r = 0.95, 0.98).

Correlations (Pearson or Spearman when appropriate) and associated 95% confidence intervals (CI) were calculated. The relationship of BMI to alignment to disease severity was evaluated using partial correlation determined from multiple regression analysis.

Results. In subjects with varus dominant knees (n = 154), the mean age was 65 years (+/- 10.8, sd) and 60% were women. In subjects with valgus dominant knees (n = 115), the mean age was 64 years (+/- 11.4) and 86% were women.

In those with varus dominant knees, BMI correlated with OA severity as reflected either by medialized joint space width [r = -0.27, 95% CI (-0.41, -0.11)] or by narrowest tibiofemoral joint space width [r = -0.29, 95% CI (-0.43, -0.14)]. However, in subjects with valgus dominant knees, BMI did not correlate significantly with either lateral joint space width (r = -0.10) or with narrowest joint space width (r = -0.13). BMI correlated with malalignment in subjects with varus knees [r = 0.26, 95% CI (0.11, 0.40)] but not in subjects with valgus knees.

An initial regression analysis (not shown) on medial OA severity to evaluate demographic factors indicated that gender, but not age, was related to joint space width. As shown in the table, the partial correlation between BMI and OA severity was 0.24, controlling for gender. The partial correlation of BMI and OA severity was reduced from 0.24 to 0.04 when varus malalignment was added to the model.

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Model R^2 (%)</th>
<th>Partial r for BMI (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1 sex, BMI</td>
<td>14.8</td>
<td>0.24 (0.16, 0.31)</td>
</tr>
<tr>
<td>Model 2 sex, BMI, alignment</td>
<td>51.5</td>
<td>0.04 (-0.04, 0.12)</td>
</tr>
</tbody>
</table>

This indicates that almost all of the effect of BMI on medial tibiofemoral OA severity was explained by the severity of varus malalignment, after controlling for gender.

Discussion. BMI and OA severity were correlated in patients with varus malalignment but not in those with valgus malalignment; these findings are consistent with and extend the clinical relevance of previous studies demonstrating that compartment load distribution is more equitable in valgus than in varus knees. In patients with varus malalignment, the relationship between BMI and OA severity was greatly reduced after accounting for the severity of malalignment, indicating that malalignment is explaining a large part of the effect of BMI on knee OA severity. It may be by amplifying and/or accelerating the cycle of medial compartment cartilage loss and varus malalignment that obesity contributes to progressive knee OA. Epidemiologic studies have provided strong evidence that obesity is linked to knee OA, but have not previously revealed mediating or intervening factors, and have not revealed reasons for the variation between lower extremity joints in the vulnerability towards developing OA in the setting of obesity.

In summary, a relationship between BMI and OA severity was present in those with varus malaligned knees but not in those with valgus malaligned knees. BMI correlated with the severity of varus malalignment. The relationship between BMI and OA severity in varus knees was reduced after accounting for the severity of malalignment. Whether it precedes or follows the onset of OA disease, varus malalignment may be an attribute of the environment of the knee that is responsible for rendering the knee most vulnerable to the effects of obesity.


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