# Synovial Macrophage Profiles In Severe Knee Osteoarthritis: Does Underlying Obesity Matter?

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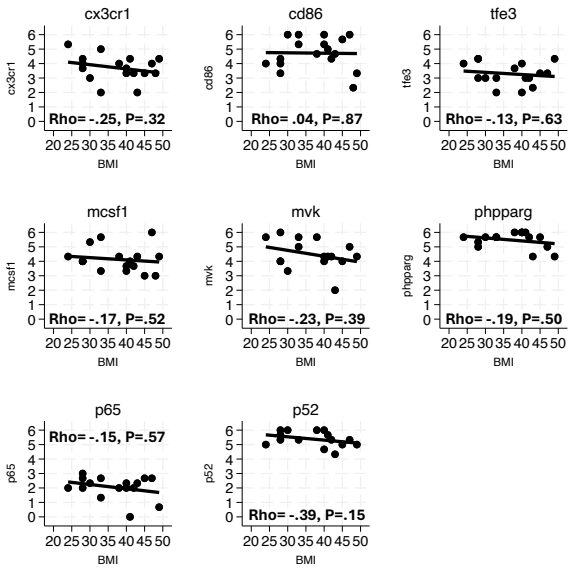
**Introduction:** When non-operative management is no longer able to manage the symptoms associated with severe knee osteoarthritis, total knee arthroplasty (TKA) is the remaining treatment option. The use of TKA is limited by complications including infection which can be difficult to manage leading to amputation and even death. While the pathology leading to infection is not completely understood, macrophages are likely involved as they are the antigen presenting cells around the knee and involved in the early immune response. Severe obesity is associated with a significantly increased risk of infection and currently used as a contraindication to TKA. While severe obesity cut-offs are often based on body-mass index (BMI), the threshold values used vary and even in patients with a BMI over 50mg/kg2, fewer than 10% would be expected to develop an infection making this a non-specific tool. To better understand the association of obesity with infection potential following TKA, we sought to describe the association of BMI with markers of macrophage expression in patients undergoing TKA.

**Methods:** Patients undergoing TKA for severe osteoarthritis were recruited. Demographic factors including age, sex, and BMI were recorded. Synovial samples were obtained at the time of surgery from the suprapatellar pouch and distal femur. These samples were processed, and immunohistochemistry was used to measure macrophage expression of CX3CR1, CD86, TFE-3, MCSF-1, MVK, PhPPAR-g, p65, and p52 on a scale from 0 to 6. Associations of BMI with these markers of macrophage expressions were assessed using scatterplots and Sperman's Rho. Cluster analysis was then used to identify two groups based on the expression of CX3CR1, CD86, MCSF-1, and MVK. The association of BMI with these cluster groups was assessed using boxplots and Wilcoxon rank-sum test.

**Results:** In total, 12 female and 5 male patients were included, ranging in age from 42 to 76 years of age. The mean BMI of the sample was 37, ranging from 24 to 49. The expression of macrophage markers did not vary between samples taken from the suprapatellar pouch and distal femur, so an average was used. There was no strong association between the markers studied with BMI (Figure). It was appreciated that there was more variation in the markers of CX3CR1, CD86, MCSF-1, and MVK so these were used to identify two clusters of patients. This produced a cluster with increased CD86 and decreased CX3CR1, MCSF-1, and MVK as well as an opposite cluster. The BMIs of these clusters did not differ significantly (P=.30).




**Discussion:** There was significant variation in synovial macrophages from patients undergoing total knee arthroplasty for severe osteoarthritis. Cluster analysis identified a group of patients with a pro-inflammatory synovial macrophage expression profile (increased CD86 and decreased CX3CR1, MCSF-1, and MVK). Neither the individual markers studied, nor the clusters were strongly associated with obesity. Given this, future work is needed to understand what underlies the association of obesity with periprosthetic infection risk as well as the role that synovial macrophages play in predisposing patients to infection. Given the significant variation seen and the important role that synovial macrophages play in antigen recognition and the initial response to these cells play in help respond to an infectious challenge, this is likely an ideal area for future research seeking to better understand the pathophysiology of periprosthetic infection.

**Significance / Clinical Relevance:** Severe obesity is currently used as a contraindication to total knee arthroplasty due to its association with an increased risk of infection. This approach is non-specific which is in line with synovial macrophage profiles described. Future work is needed to better understand the association of severe obesity with periprosthetic infection.