

Not just loading and age: the dynamics of osteoarthritis, obesity and inflammation

Body fat is not an inert structure

“the old paradigm of OA being a degenerative, wear-and-tear disease of older age, and not an inflammatory disease, has been challenged”

Obesity is a well recognised risk factor for osteoarthritis (OA).¹ It is commonly believed that obesity affects joints through loading. However, there must be additional mechanisms since, for decades, obesity has been known to be a strong risk factor for hand OA. Given that we do not walk on our hands, an effect of obesity through loading of the joints cannot be the whole explanation. An understanding of the potential mechanisms by which obesity affects joints is important for optimising the treatment and prevention of OA.

Work over the past decade using magnetic resonance imaging has enabled the assessment of factors affecting joints across the spectrum of the disease, from normal asymptomatic joints to symptomatic OA.¹ This has made it possible to examine the effect of obesity on joints, and to untangle the issue of whether obesity causes OA or whether OA-related pain causes obesity through modification of lifestyle behaviours and consequent weight gain. This work has shown that obesity is a causative factor in the development of OA, with increased weight being associated with early articular cartilage damage, well before symptoms develop.¹ Obesity is an important risk factor for OA across a wide range of joints, including hands, back, hip and knee.

Having established the importance of obesity as a causative factor for OA, it is important to consider potential mechanisms and to recognise that measures of obesity, such as weight and body mass index, have limited usefulness because they do not provide information regarding body composition. For example, body composition may be very different in two men with an identical body mass index of 30 kg/m²: one may have a very high proportion of muscle, while the other may have a very high proportion of fat. Several studies have examined the effect of body composition, particularly fat mass, on joint health.¹ A large body of evidence has shown that an increase in fat mass is associated with pre-clinical OA.¹ Increased fat mass is also associated with faster loss of knee cartilage and an increased likelihood of joint replacement. An increase in fat mass is also associated with more back pain and disability² and foot pain.³

The findings that increased fat mass is associated with early through to late OA, independent of obesity, suggest that the effect of obesity on the joint may be via metabolically driven inflammation. It is well recognised that body fat is not an inert structure but rather a highly metabolically active tissue that produces inflammatory molecules, including cytokines and adipokines, that have been shown to damage joints.⁴ Circulating levels



of inflammatory cytokines⁵ and low-grade synovitis are associated with cartilage loss.⁶ Higher levels of the adipokine leptin are also independently related to increased cartilage loss, suggesting a systemic mechanism for the effect of obesity on knee cartilage.⁷ Thus the old paradigm of OA being a degenerative, wear-and-tear disease of older age, and not an inflammatory disease, has been challenged.

So what are the implications of these findings? For weight-bearing joints, as obesity affects joints through both mechanical loading and metabolically driven inflammation, the effects are synergistic; the joint that is being loaded, rather than being healthy, is also subjected to low-grade inflammation — a double “hit”. Thus if a patient is carrying 20 kg extra weight, they are not carrying 20 kg of inert fat. The individual is carrying 20 kg of metabolically active tissue that is not only overloading the joint, but also producing inflammatory molecules resulting in a more vulnerable joint being loaded. The inflammatory mechanisms may also contribute to some of the obesity-related risk for non-weight-bearing joints.

The inflammatory mechanism for obesity-related damage to joints highlights the importance of preventing obesity in early life to avoid early joint damage. Such damage sets up a vicious cycle of further joint damage through both inflammation and loading. It may also contribute to the increased risk of cardiovascular disease seen in those with OA.⁹ Preventing early weight gain is potentially a more achievable and effective option than weight loss in later life.^{9,10} Once disease is established, weight maintenance may be a more feasible goal than weight loss for minimising pain and structural progression in joints such as the knee.^{1,9} With our increasingly obese population and its associated burden of osteoarthritis, novel therapies aimed at targeting inflammatory pathways warrant further investigation.

Competing interests: No relevant disclosures.

Provenance: Commissioned; externally peer reviewed. ■

© 2016 AMPCo Pty Ltd. Produced with Elsevier B.V. All rights reserved.

References are available online at www.mja.com.au.

Flavia M Cicuttini
MSc, FRACP, PhD

Anita E Wluka
MBBS, FRACP, PhD

Monash University,
Melbourne, VIC.

flavia.cicuttini@monash.edu

doi: 10.5694/mja15.01069

Podcast with Professor Flavia Cicuttini is available at www.mja.com.au/multimedia/podcasts

- 1 Mezhov V, Ciccuttini FM, Hanna FS, et al. Does obesity affect knee cartilage? A systematic review of magnetic resonance imaging data. *Obes Rev* 2014; 15: 143-157.
- 2 Urquhart DM, Berry P, Wluka AE, et al. 2011 Young Investigator Award winner: increased fat mass is associated with high levels of low back pain intensity and disability. *Spine* 2011; 36: 1320-1325.
- 3 Tanamas SK, Wluka AE, Berry P, et al. Relationship between obesity and foot pain and its association with fat mass, fat distribution, and muscle mass. *Arthritis Care Res (Hoboken)* 2012; 64: 262-268.
- 4 Gomez R, Lago F, Gomez-Reino J, et al. Adipokines in the skeleton: influence on cartilage function and joint degenerative diseases. *J Mol Endocrinol* 2009; 43: 11-18.
- 5 Pelletier JP, Raynaud JP, Caron J, et al. Decrease in serum level of matrix metalloproteinases is predictive of the disease-modifying effect of osteoarthritis drugs assessed by quantitative MRI in patients with knee osteoarthritis. *Ann Rheum Dis* 2010; 69: 2095-2101.
- 6 Roemer FW, Guermazi A, Felson DT, et al. Presence of MRI-detected joint effusion and synovitis increases the risk of cartilage loss in knees without osteoarthritis at 30-month follow-up: the MOST study. *Ann Rheum Dis* 2011; 70: 1804-1809.
- 7 Attur M, Krasnokutsky-Samuels S, Samuels J, Abramson SB. Prognostic biomarkers in osteoarthritis. *Curr Opin Rheumatol* 2013; 25: 136-144.
- 8 Hubert HB, Feinleib M, McNamara PM, Castelli WP. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. *Circulation* 1983; 67: 968-977.
- 9 Lombard CB, Deeks AA, Teede HJ. A systematic review of interventions aimed at the prevention of weight gain in adults. *Public Health Nutr* 2009; 12: 2236-2246.
- 10 Messier SP, Mihalko SL, Legault C, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. *JAMA* 2013; 310: 1263-1273.