RBO REVISTA BRASILEIRA DE ORTOPEDIA
www.rbo.org.br

Update Article

Is osteoarthritis a mechanical or inflammatory disease?☆,☆☆

*Márcia Uchôa de Rezende**, *Gustavo Constantino de Campos*

Institute of Orthopedics and Traumatology, Hospital das Clínicas, School of Medicine, University of São Paulo, São Paulo, SP, Brazil

ARTICLE INFO

Article history:
Received 14 March 2013
Accepted 19 March 2013

Keywords:
Osteoarthritis
Inflammation
Arthritis
Chronic disease
Mechanics

ABSTRACT

Traditionally considered "wear and tear" disease, the pathogenic mechanisms of osteoarthritis have not yet been elucidated. The increasing number of articles demonstrating the influence of inflammatory factors in the onset and progression of the disease currently raises great debate in the literature about the importance of each of the factors involved in the disease. Even the choice between the terms "Osteoarthritis" and "Osteoarthrosis" generates controversy, since the first term implies the presence of inflammation as the key generator of the disease, and the latter denotes a degenerative/mechanical causal factor. The aim of this revision article is to promote a debate on the influence of inflammatory factors and mechanical factors in the pathogenesis of OA.

A osteoartrite é uma doença mecânica ou inflamatória?

Palavras-chave:
Osteoartrite
Inflamação
Artrite
Doença crônica
Mecânica

RESUMO

Classicamente considerada uma doença de *wear and tear* (desgaste), a osteoartrite ainda não tem elucidados todos os seus mecanismos patogênicos. O crescente número de artigos que demonstram a influência dos fatores inflamatórios no surgimento e na evolução da doença suscita, atualmente, grande debate na literatura sobre a importância de cada um dos fatores envolvidos. Até mesmo a escolha dos termos osteoartrite e osteoartrose gera polêmica, uma vez que o primeiro implica a presença da inflamação como fator primordial gerador da doença e o último denota um fator causal degenerativo/mecânico. O objetivo deste artigo é promover um debate sobre a influência dos fatores inflamatórios e dos fatores mecânicos na patogênese da OA.

☆ Please cite this article as: de Rezende MU, de Campos GC. A osteoartrite é uma doença mecânica ou inflamatória? Rev Bras Ortop. 2013;48:471–474.

☆☆ Work performed at the Institute of Orthopedics and Traumatology, Faculty of Medicine, University of São Paulo, São Paulo, SP, Brazil.

* *Corresponding author.*
E-mail: murezende@uol.com.br (M.U. de Rezende).

2255-4971 http://dx.doi.org/10.1016/j.rboe.2013.12.002

Introduction

The concept that osteoarthritis (OA) is an inevitable consequence of aging, i.e. wear and tear on the joints due to use, is gradually being left behind. The term "degenerative joint disease", which is still greatly used, denotes the idea of futility and inevitability and does not express the true complexity of the problem. In view of the current knowledge, two sets of factors that seem to play a fundamental role in the development of OA have arisen: mechanical and inflammatory factors. However, there are divergent views in the literature regarding the importance to be given to each of these. The aim of this article was to promote a debate on the influence of inflammatory factors and mechanical factors on the pathogenesis of OA.

Taking the role of "devil's advocate", we firstly try to convince readers that OA is an inflammatory disease. We then present arguments in favor of treating it as a mechanical disease. We invite readers, before starting to read onwards, to choose just one of these theories. At the end, we believe that some readers will surprise themselves by changing their opinion after seeing the strong arguments on both sides.

Osteoarthritis is an inflammatory disease

The inflammatory process found in OA has been studied for several decades.[1,2] According to some recent studies,[3,4] OA behaves like an autoinflammatory disease, caused by responses mediated by chondrocytes and synoviocytes. The serum and synovial levels of inflammatory cytokines are higher in patients with OA.[5,6] There is much clinical evidence of the importance of inflammation in the pathogenesis of the disease, which even provides new potential therapeutic targets.[7]

Among the clinical signs seen in OA in any part of the body, there is an increase in joint volume, probably due to synovial effusion or thickening. This is an irrefutable sign of the presence of synovitis. There are increasing numbers of studies in the literature correlating synovitis with OA. In a search in PubMed using the terms *osteoarthritis* and *synovitis*, we found 1253 published papers with this association. Patients with OA frequently present episodes in which the condition becomes acute, known as flare-ups, which follow a course that includes joint effusion, pain when resting and/or morning stiffness.

Magnetic resonance imaging (MRI) with contrast and ultrasonography (US) are valid and efficient tools for studying synovitis.[8] Synovitis and joint effusion increase the risk of loss of cartilage in knees that initially do not have OA.[9] By means of arthroscopy, Ayral et al.[10] observed that the greater the degree of synovitis encountered was, the greater the chance of joint deterioration would be. In another study, great presence of inflamed tissue was observed in histological sections from osteoarthritic joints.[11]

In an experimental model for OA caused by means of collagenase-induced lesions,[12] the group in which the macrophages of the synovium were depleted before OA was induced did not present degradation. This signifies that macrophages have a fundamental role in the pathogenesis of OA and are not just a consequence of it. The stress mechanism itself often functions like a veritable cytokine.[13] Mechanical stress is picked up and interpreted by mechanical receptors, which then activate inflammatory cascades, exactly in the same way as occurs in activation caused by cytokines.[14]

Among patients with OA, a phenotype in which the disease accompanies metabolic disorders such as diabetes or obesity[15,16] clearly exists. Adipose tissue is capable of producing adipokines and other inflammatory mediators, which increase the levels of inflammatory activity throughout the body,[17] and even in osteoarthritic joints.[18] Obese patients present twice as much risk of presenting OA in their hands, which signifies that the greater incidence of OA in the knees and hips of obese individuals cannot be attributed only to their greater weight.[19]

Finally, it is known that aging increases the cellular response to inflammatory factors.[20] Cell senescence increases cytokine production and thus aging causes a state of chronic inflammation that is characterized as low-intensity, systemic and subclinical. To describe this state, Franceschi et al. introduced the term inflammaging,[21] as a combination between inflammation and aging.

Osteoarthritis is a mechanical disease

Saying that a disease is mechanical means that it is related to movement and physical forces, or is caused by these. This is precisely what leads to OA, i.e. increased physical force in localized areas of a joint. OA is a joint's pathophysiological response to a mechanical injury.[22] It represents an attempt by the joint to correct an abnormal mechanical stress and repair the injury resulting from this. Although some authors consider that increased levels of cytokines, free radicals and degradative enzymes in the joint are the cause of OA,[2–4,16] there is evidence indicating that in fact all inflammatory responses are the result of attempts to repair osteoarthritic joints.[23]

Among the causes that may lead to an abnormal increase in forces in localized areas of the joint, the following can be observed: (1) congenital or acquired abnormal anatomy, such as congenital misalignment or a meniscal or anterior cruciate ligament injury, which leads to increased stress even under physiological loads; (2) excessive loading, like in obese individuals; (3) a combination of factors, which is the commonest scenario. Moreover, it is not the misalignment that causes OA, but its effect of concentrating the intra-articular stress. It is not the estrogen deficiency or a genetic abnormality in itself, but the effects that stem from these alterations that cause the joint tissues to lose the ability to protect themselves adequately against loads that are often physiological.

Abnormal mechanics cause OA. Most animal models use focused load increases to cause OA (meniscal injury or resection of the ACL).[24] Wu et al.[25] caused OA in rabbits through inducing misalignment with an increase in varus moment. Animal models that do not cause injury (for example, using iodine acetate) do not resemble OA. There are no models with cytokines or inflammatory factors.

In humans, many studies have correlated meniscal injuries with OA.[26] Occasional meniscal injuries occur in 30–60% of individuals over the age of 50 years,[27] and their occurrence