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Early evolving joint degeneration by cartilage trauma is primarily mechanically controlled

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ABSTRACT

Background: Mechanical and inflammatory processes add to osteoarthritis (OA). To what extent both processes contribute during the onset of OA after a cartilage trauma is unknown. This study evaluates whether local cartilage damage leads to focally confined or more generalized cartilage damage with synovial inflammation in the early development of joint tissue degeneration.
Methods: In nine goats, cartilage damage was surgically induced on the weight bearing area of exclusively the medial femoral condyle of the right knee joint. The other tibio-femoral compartments, lateral femoral condyle and lateral medial tibial plateau, were left untouched. The contralateral left knee joint of each animal served as an intra-animal control. Twenty weeks post-surgery changes in cartilage matrix integrity in each of the four compartments, medial and lateral synovial tissue inflammation, and synovial fluid IL-1β and TNFα were evaluated.
Results: In the experimental medial femoral plateau, significant macroscopic, histologic, and biochemical cartilage damage was observed versus the contralateral control compartments. Also the articulating cartilage of the experimental medial tibial plateau was significantly more damaged. Whereas, no differences were seen between the lateral compartments of experimental and contralateral control joints. Synovial tissue inflammation was mild and only macroscopically (not histologically) significantly increased in the experimental medial compartments. Synovial fluid IL-1β level was not different between experimental and contralateral control joints, and TNFα was overall beneath the detection limit.
Conclusions: Local cartilage damage is a trigger for development of OA, which in early onset seems primarily mechanically driven. Early treatment of traumatic cartilage damage should take this mechanical component into consideration.

1. Introduction

Osteoarthritis (OA) is a chronic, progressive musculoskeletal disorder characterized by joint tissue degeneration causing pain and loss of function. Worldwide about 10% of men and 20% of women suffer from symptomatic OA according to the World Health Organization and the estimated life time risk of developing OA is over 10% [1]. However, numbers are muddled due to difficulties defining OA and especially determining the specific onset of OA [2].

There are various pathophysiological processes responsible for the onset of OA. OA is seen as a multifactorial heterogeneous disease with multiple risk factors, including primary cartilage damage due to e.g. trauma or mechanical overload [3]. Moreover, several different phenotypes of OA onset exist, each with their own disease characteristics [4,5]. In general the disease is considered to be driven by the combination of mechanical and inflammatory processes. It is still unclear to what extent both processes contribute to the onset of OA in different phenotypes, illustrated by the ongoing debate on the role of mechanical mechanisms [6] versus the contribution of the inflammatory systems [7] in the pathophysiological process of OA. It is sensible to assume that different phenotypes have different mechanisms of onset in which either mechanical or inflammatory processes will dominate.

A mechanical property of healthy cartilage is its capacity to deform under weight-bearing conditions in order to distribute load sufficiently. Change or loss of this property due to cartilage damage will cause increased intra-articular stress, recognized as “over-loading” and will lead to progressive cartilage matrix breakdown, eventually resulting in

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cartilage damage, due to increased load and shear forces on the cartilage surface [8]. This vicious circle, initiated by tissue changes, leads to a continuously changing biomechanical environment and progressive joint tissue damage [6].

On the other side, inflammatory mechanisms and synovitis play a role in varying degrees in OA [7]. As a result of cartilage damage, debris triggers the synovial tissue, which will react with release of inflammatory factors into the synovial fluid [9]. These mediators will alter chondrocyte activity leading to release of a multitude of soluble factors involved in cellular activity and cartilage matrix breakdown, including pro-inflammatory cytokines (e.g. IL-1β, TNFα) and tissue destructive enzymes (collagenases and aggrecanases) [10].

According to the current guidelines of the EULAR [11] and OARSI [12], treatment of symptomatic early joint degeneration includes non-pharmacological (e.g. education, physiotherapy) and pharmacological (e.g. acetaminophen, NSAIDs) treatment. Depending on the actual processes involved, these more generalized treatment guidelines might be more focused on specific onset or disease progress of different OA phenotypes.

To our knowledge, it has never been studied whether local cartilage damage will develop into early OA mostly by mechanical factors and remains focally confined in one tibio-femoral compartment ('kissing-lesion'), or will spread through the joint supported by significant involvement of soluble mediators and synovial inflammation (see Figure 1a for a representation of this hypothesis).

2. Materials and methods

2.1. Animals

Nine skeletally mature milk goats (female, 72.9 ± 2.9 kg, age 2.3 ± 0.2 years, mean ± SD) were obtained from a commercial Dutch breeder. Animals were housed in two groups of four and five animals each, freely walking in pens of approximately 20 m^2. There were no dietary restrictions with water ad libitum. The Utrecht University Medical Ethical Committee for animal studies approved the experiment (DEC2009.III.01.002).

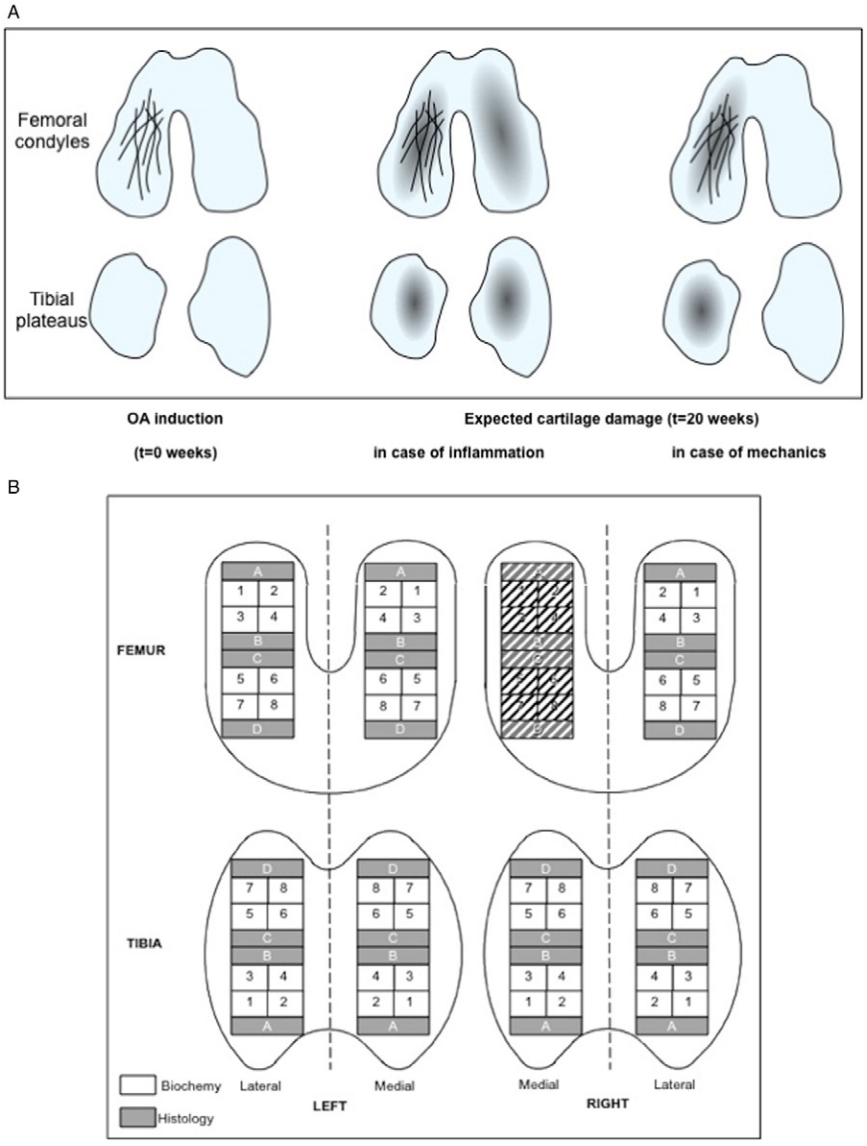

Figure 1. Representation of the induced cartilage trauma, and the hypothetical spread of the degeneration process throughout the whole joint; in the case of a merely biochemical or respectively biomechanical processes. Cartilage samples. Schematic overview of cartilage samples harvested from the four compartments of both the experimental and contralateral control joint. Every sample was taken from the weight bearing area of the femoral condyles and tibial plateaus. The locations were identically paired between the medial and lateral compartment, femur and tibia and between the experimental and contralateral control joints. The dashed area indicates the surgically damaged compartment.