Role of acute trauma in development of osteoarthritis

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Abstract

Two canine acute transarticular loading models have been developed to study the role of acute traumatic cartilage damage in the development of osteoarthritis. One model involves damage to a closed joint and has the advantage of maintaining normal joint biology. The second model involves impaction of an open joint with direct visualization of the cartilage and has the advantages of being able to change the placement, intensity, and geometry of the impaction. Comparison of preliminary histochemical data at 2 weeks and 3 months for the open joint model with previously published data on the closed joint model is consistent with the two models having similar initial features that include surface cracks and step fractures of the zone of calcified cartilage. The early changes include loss of proteoglycan, expression of the pro-inflammatory markers such as TNF-α and IL-1β, and the metalloprotease stromelysin. By 3 months, cloning is present. The models will be useful in evaluating two hypotheses: one, that there is a threshold of damage that must be exceeded before the lesions become progressive and two, the cracks in the zone of calcified cartilage contribute to progression of osteoarthritis by acting as sites of endochondral ossification and thereby decreasing cartilage thickness.

Introduction

Acute trauma to articular cartilage is one of the few identified factors that contribute to the development of osteoarthritis. In large studies, 13 to 18% of patients receiving a total hip or total knee have had an identifiable incidence of acute trauma to the joint [1]. However, other than the case where intraarticular fractures with displacements greater than 2 mm, which produce high local stresses, are produced [2], the mechanism of how trauma induces osteoarthritis is unknown. Two canine models have been developed for investigating the process. The original model involves inducing damage by loading the patella with a weight dropped onto the closed joint from a height of up to 2 meters [3, 4]. The resulting reproducible damage to the distal pole of the patella consists of splits in the surface of the cartilage, some cell death, and cracks in the zone of calcified cartilage-bone interface.

In a series of experiments, groups of 4 to 6 adult male mongrel canines have been followed for up to 1 year and investigated biochemically and histologically [3, 4]. Acute bench testing of specimens followed by scanning electron microscopy was also used to characterize the nature of damage to the zone of calcified cartilage-cartilage interface in this
type of impact [4, 5]. Additionally, multi-layer elastic contact models have been developed and used to investigate the mechanism of damage [6, 7]. However, there is a need for an additional system that will allow a more flexible placement of the impact and be amenable to changes in forces and geometries.

**Methods**

In this new model, the mature male canine joint is surgically opened under general anesthesia, the patella is dislocated medially, and a 7 mm smooth Steinmann’s pin is placed across the femoral condyle at the level of the old epiphysis. The limb is held rigidly to the drop tower apparatus by a special support frame [4]. The femoral condyles are impacted at up to three different locations (2 lateral, 1 medial) with a spherical indentor. After photography, the pin is removed, the patella is relocated and the joint closed. The opposite limb is treated in the same manner except for the impaction. Groups of 4 to 6 animals have been evaluated by histochemistry at 2 and 12 weeks after impaction. Formaldehyde-fixed, formic acid decalcified, and paraffin embedded sections are stained with Safranin O, fast green or immunochemical stains [4, 8].

**Figure 1**

Schematic representation of the different phases of the responses of articular cartilage after acute trauma.

A) **Acute Damage:**
1) Surface fractures, 2) Cell damage, 3) Microscopic matrix damage, 4) Fractures from ZCC into cartilage, 5) Stair step fracture of ZCC, 6) Surface disruption, 7) Subchondral bone damage into marrow space.

B) **Early Response:**
1) Factors diffuse in from synovium, 2) Cell death or repair, 3) Matrix damage accelerates, 4) Repair of ZCC begins, 5) Stair step fractures begin to heal, 6) Factors may diffuse in from subchondral bone.

C) **Intermediate (Degenerate) Response:**
1) Cracks propagate, 2) Cells clone, 3) Enhanced matrix damage, 4) Cell secretes factors, 5) Endochondral repair occurs, 6) Increased area of proteoglycan loss.

D) **Healing Phase:**
1) Surface cracks stabilize, 2) Cell clones stabilize, 3) Microdamage stabilize, 4) Crack fills in, 5) Step off of ZCC are healed, 6) Region or proteoglycan depletion is diminished, 7) Subchondral bone stabilizes.