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Bone 38 (2006) 342–349

BONE

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Role of endochondral ossification of articular cartilage and functional adaptation of the subchondral plate in the development of fatigue microcracking of joints

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Received 24 May 2005; revised 27 July 2005; accepted 23 August 2005
Available online 4 November 2006

Abstract

The mechanisms that regulate functional adaptation of the articular ends of long bones are poorly understood. However, endochondral ossification of articular cartilage and modeling/remodeling of the subchondral plate and epiphyseal trabeculae are important components of the adaptive response. We performed a histologic study of the distal end of the third metacarpal/metatarsal bone of Thoroughbreds after bones were bulk-stained in basic fuchsin and calcified sections were prepared. The Thoroughbred racehorse is a model of an extreme athlete which experiences particularly high cyclic strains in distal limb bones. The following variables were quantified: microcrack boundary density in calcified cartilage (N.Cr/B.Bd); blood vessel boundary density in calcified cartilage (N.Ve/B.Bd); calcified cartilage width (Cl.Cg.Wi); duplication of the tidemark; and bone volume fraction of the subchondral plate (B.Ar/T.Ar). Measurements were made in five joint regions (lateral condyle and condylar groove; sagittal ridge; medial condylar and condylar groove). N.Cr/B.Bd was site-specific and was increased in the condylar groove region; this is the joint region from which parasagittal articular fatigue (condylar) fractures are typically propagated. Formation of resorption spaces in the subchondral plate was co-localized with microcracking. N.Ve/B.Bd was also site-specific. In the sagittal ridge region, N.Ve/B.Bd was increased, Cl.Cg.Wi was decreased, and B.Ar/T.Ar was decreased, when compared with the other joint regions. Multiple tidemarks were seen in all joint regions. Cumulative athletic activity was associated with a significant decrease in B.Ar/T.Ar in the condylar groove regions. N.Cr/B.Bd was positively correlated with B.Ar/T.Ar ($P < 0.05$, $r_s = 0.29$) and N.Ve/B.Bd was negatively correlated with B.Ar/T.Ar ($P < 0.005$, $r^2 = 0.14$) and Cl.Cg.Wi ($P < 0.05$, $r^2 = 0.07$). We conclude that endochondral ossification of articular cartilage and modeling/remodeling of the subchondral plate promote initiation and propagation of site-specific fatigue microcracking of the joint surface, respectively, in this model. Microcracking of articular calcified cartilage likely represents mechanical failure of the joint surface. Propagation of microcracks into the subchondral plate is a critical factor in the pathogenesis of articular condylar fatigue (stress) fracture. Functional adaptation of the joint likely protects hyaline cartilage from injury in the short-term but may promote joint degeneration and osteoarthritis with ongoing athleticism.

Keywords: Fatigue; Microcracking; Targeted remodeling; Calcified cartilage; Subchondral plate

Introduction

Articular parasagittal fracture of the distal end of the third metacarpal/metatarsal bone (Mc-III/Mt-III) or condylar fracture is a common injury in racing Thoroughbred horses, which has been recognized clinically for many years [1]. The Thoroughbred horse is capable of extreme athletic performance and can run at speeds exceeding 15 m/s; during high-speed running, the bones of the distal limb are exposed to large cyclic strains, which can exceed −5,000 με at the midshaft of the third metacarpal [2]. Athletic activity induces extensive and rapid functional adaptation of both the shaft and the subchondral bone in the distal end of the Mc-III/Mt-III bone within a few months [3,4].

Functional adaptation of bone occurs during life and also over evolutionary time [5]. Loading does not have to be great to induce microcracking, if it is rapidly applied [6]. While bones may be well adapted to normal cyclic loading, bone may not effectively resist propagation of microcracking, especially if

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8756-3282/$ - see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.bone.2005.08.020

abnormal or atypical loads are applied [5,7]. In the distal metaphysis of the Mc-III/Mt-III bone of the Thoroughbred horse, proximal to the subchondral plate, the cancellous bone is arranged in sheets of plate-like trabeculae with relatively thin cross-struts [8]. The sheets of bone run in a dorso-palmar/plantar direction [8]. This structure effectively resists the forces of locomotion but does not resist development of a parasagittal fracture once the cortical shell of the distal end of the bone has been disrupted [5]. Although incomplete condylar fractures have been recognized clinically for some time [1,9], it is only recently that it has been widely recognized that this fracture propagates from a specific region of the joint surface. These parasagittal fractures arise from the palmar/plantar region of the condylar groove (Fig. 1) between the sagittal crest and the condyles of the distal joint surface [9]. Accumulation and coalescence of microcracks in adapted subchondral bone likely propagate growth of a critical fracture line, which by lengthening and widening weakens the cortical shell until an overt fracture develops during normal racing activity [10–12].

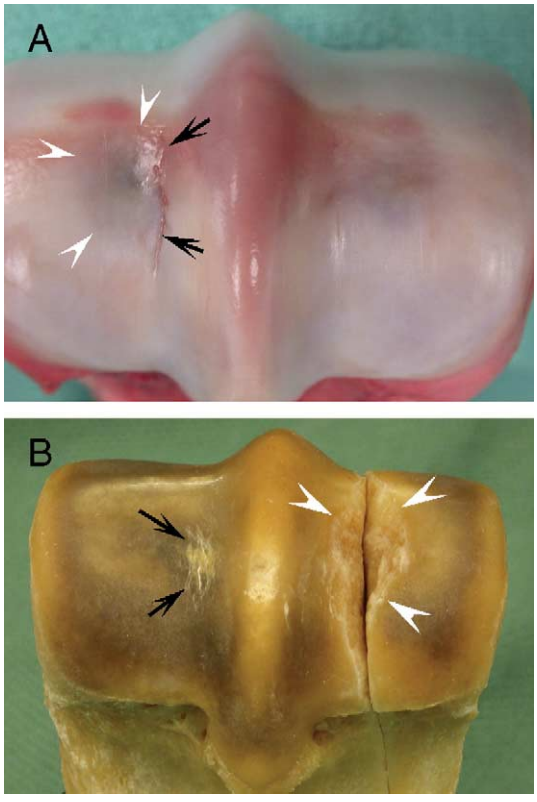

Fig. 1. Photographic view of the palmar distal region of the distal joint surfaces of the Mc-III bones from a 3-year-old male Thoroughbred. (A) In the right Mc-III bone, a parasagittal defect can be seen in the articular cartilage of the lateral condylar groove (black arrows). Adjacent to this lesion is circular area of cartilage degeneration in the lateral condylar (white arrow heads). A similar lesion is also present to a lesser extent in the medial condyle. Parasagittal linear wear lines in the articular cartilage are also visible. (B) In the left Mc-III bone, a parasagittal condylar fracture is present in the lateral condylar groove (white arrowheads). In the medial condylar groove, a branching array of subchondral cracks can be seen (black arrows). In the lateral condylar groove, comminution of this subchondral bone developed during propagation of the fracture. The articular cartilage was removed by treatment with 0.1 M NaOH to permit the articular surface of the subchondral bone to be examined.

In 1999, Riggs et al. [10] suggested that the cracks that develop in the cortical shell of the distal end of the Mc-III/Mt-III develop preferentially in the condylar groove as a consequence of functional adaptation of the joint surface to athletic activity. However, the specific mechanism that promotes site-specific induction and propagation of microcracking in the subchondral bone of the condylar groove region of the joint is not understood.

The purpose of the present study was to determine whether specific histologic features of the subchondral bone of the distal end of the Mc-III/Mt-III in Thoroughbred horses with and without condylar fatigue fractures were associated with the development of subchondral microcracking in the condylar groove region of the joint. We hypothesized that development of subchondral microcracks would be associated with specific regional changes in the microscopic architecture of the subchondral plate of the distal joint surface of the Mc-III/Mt-III bone.

Methods

Horses

Mc-III/Mt-III bones were collected from 12 Thoroughbred racehorses that had sustained a serious orthopedic injury while racing which was severe enough to result in euthanasia. Age and racing history were obtained. The nature of the orthopedic injury was confirmed on dorso-palmar/plantar and medial–lateral radiographs of the Mc-III/Mt-III bone. Bones were stored at −20°C for further processing.

Specimen preparation

Bones were transected at the distal portion of the metaphysis and incubated in 0.1 M NaOH until all the articular cartilage and soft tissue had been removed [11] and then fixed in 70% ethanol. This treatment retains calcified cartilage with the bone specimen. Oblique frontal bone blocks of the distal end of the Mc-III/Mt-III bone [13], approximately 1 cm thick, centered on the region-of-interest in the subchondral bone of the palmar/plantar part of the joint were prepared using a band saw. If a condylar fracture was present, reduction of the fracture was maintained with cyanoacrylate glue during cutting. The blocks were notched to maintain lateral to medial orientation. Bone blocks were then bulk-stained in a 1% basic fuchsin in a graded series of ethanols (80%, 90%, 100%) for a total staining time of 18 days under vacuum (20–40 mm Hg) [14]. This technique stains osteocyte lacunae and canaliculi and stains microcracks that existed before histologic sectioning, thus allowing them to be differentiated from unstained artifactual damage induced during sectioning [14]. This technique also stains blood vessels within calcified cartilage. After the bone blocks were embedded in polymethylmethacrylate, calcified oblique frontal bone sections of the distal joint surface were cut and ground to a thickness of approximately 125 μm (Exakt Technologies, Oklahoma City, OK).

Histomorphometry

The subchondral bone of the distal articular surface of the Mc-III/Mt-III bone was divided into five regions-of-interest: (1) lateral condyle; (2) lateral condylar groove; (3) sagittal ridge; (4) medial condylar groove; (5) medial condyle (Fig. 2). These regions were established by identifying the point that was equidistant from the tip of the sagittal ridge and the bottom of the condylar groove as the interface between the condylar groove and sagittal ridge regions. The same distance abaxial from the bottom of the condylar groove determined the interface between the condylar groove region and the condyle region.

Morphometric analysis was performed using bright-field microscopy at 100× magnification and image analysis software (Scion Corporation, Frederick, MD). For each region-of-interest, the following features were studied: (1)