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Review article

How to establish an expected animal model of post-traumatic osteoarthritis?

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ABSTRACT

Background: Animal models of osteoarthritis (OA), including post-traumatic osteoarthritis and spontaneous osteoarthritis, have been established in many ways. In recent years, there have been many reports in various foreign academic journals, but animal models of post-traumatic osteoarthritis (distinct from spontaneous osteoarthritis) have rarely been established or summarized in these reports. Animal models of post-traumatic osteoarthritis show different characteristics depending on the animal species and modeling methods used, which is why we have written this article.
Objective: To summarize the research progress and research status of animal models of post-traumatic osteoarthritis.
Methods: A retrospective review of the animal model of post-traumatic osteoarthritis (OA) was conducted on the basis of reports retrieved from the PubMed database with the keywords for searching "animal model, post-traumatic osteoarthritis (PTOA)" from October 2006 to October 2016 and confided English language. A total of 80 academic articles on the study of animal models of traumatic osteoarthritis were retrieved, and 34 of them were included in this literature review after reading the free full-text of them.
Results: Different PTOA models based on different modeling methods and different animal species had their own characteristics. Different modeling methods should be selected according to different modeling animals.
Conclusions: Considering the project funds, experimental objectives and technical conditions, appropriate experimental animal and modeling method should be selected based on synthetic considerations to obtain an appropriate PTOA model and ideal experimental results.

1. Introduction

Osteoarthritis (OA) is a common inflammatory joint disease that affects a growing portion of the elderly and has a strong socio-economic impact.[1] Because the pathogenesis and etiological factors of post-traumatic osteoarthritis are not clear, the lack of effective clinical diagnosis and treatment measures for the recovery of such patients has caused difficulties; therefore, it is necessary and urgent to study OA by establishing a traumatic osteoarthritis animal model.

Animal models of post-traumatic osteoarthritis can be established by selecting different animal species through a variety of artificial means to induce progressive cartilage injury, subchondral bone reconstruction, osteophyte formation and soft tissue inflammation around the joints and other pathological processes. In this review, we summarize the research methods and current research situation of animal models of post-traumatic osteoarthritis, covering nearly ten years of foreign academic papers, to provide appropriate reference methods for modeling post-traumatic osteoarthritis animal models in future studies.

2. Data and methods

2.1. Source

First, the authors searched the PubMed database from October 2006 to October 2016 for animal models of post-traumatic osteoarthritis using the keyword search of "animal model, post-

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traumatic osteoarthritis (PTOA)" with an English language restriction.

2.2. Inclusion criteria

The eligible literature should describe the related experimental study work and summarize the establishment and use of animal models of post-traumatic osteoarthritis.

2.3. Exclusion criteria

The exclusion criteria were an unreasonable experimental design and experimental methods and poorly described or repetitive description of the establishment of animal models.

2.4. Quality control

According to the inclusion criteria and exclusion criteria, the first and second authors read the references carefully to obtain qualified literature.

2.5. Search results

A total of 80 academic papers studying animal models of post-traumatic osteoarthritis were retrieved, and 34 of them were included in this review after reading the free full-text articles.

3. Results

3.1. Extra-articular induction: tibial compression overload model (7/34)

In 2012, Christiansen et al[2] used C57BL/6N mice and an overload cycle of the tibial compression method using a tibial compression system that consisted of two custom-built loading platens to establish a post-traumatic animal model. The bottom platen held the knee flexed, and the top platen positioned the foot with the ankle at approximately 30°.Then, the right leg of each mouse was subjected to a single dynamic axial compressive load, which caused a transient anterior subluxation of the tibia relative to the distal femur (Fig. 1). In view of the normal activities of the joint stress environment of articular cartilage, this modeling method is of great significance. Increasing or decreasing joint stress artificially could result in PTOA. Bone matrix damage is caused when stress artificially increases or decreases. Due to compensatory hypertrophy and degeneration of cartilage cells, cartilage degeneration of the entire animal cartilage joint occurs.

Satkunananthan et al,[3–5] used C57BL/6N mice to successfully replicate the PTOA model in their experiments. Killian et al[6] successfully established a model by subjecting Flemish Giant rabbits to a blunt force insult to the tibiofemoral joint with compression axial overload. Tochigi et al[7] successfully molded the elbow joint PTOA model using agricultural pigs. The elbow joints received an axial compression overload. Borrelli et al[8] changed the position of the overload. New Zealand White rabbits received compression on the medial condyle of a femur to successfully simulate the course of human PTOA.

3.2. Intra-articular surgery

3.2.1. Anterior cruciate ligament transection, ACLT model (4/34)

In 1973, Pond et al[9] performed anterior cruciate ligament transection surgery in one of the hind limb knees of 10 dogs, and the contralateral joints were used as controls. The animals were sacrificed at different times 1–26 weeks after surgery. Radiological and pathologic examinations showed that the humanoid PTOA model was successfully established (Fig. 2). This modeling principle generally indicates that the tibia should be constrained from the anterior cruciate ligament to limit its excessive movement. After the anterior cruciate ligament of the animal model was removed, forward displacement of the tibial and hind limb knee joint rotation inward increased the flexion and extension processes of the animal's hind limb knee, resulting in joint stability destruction, eventually causing PTOA.

The canine ACLT model demonstrated that the animals recovered to a preoperative level 5 months after ACLT surgery by observing their ground reaction force (GRFs) and hind knee joint mechanics data. In 2005, Boyd et al[10] divided 13 cats into three

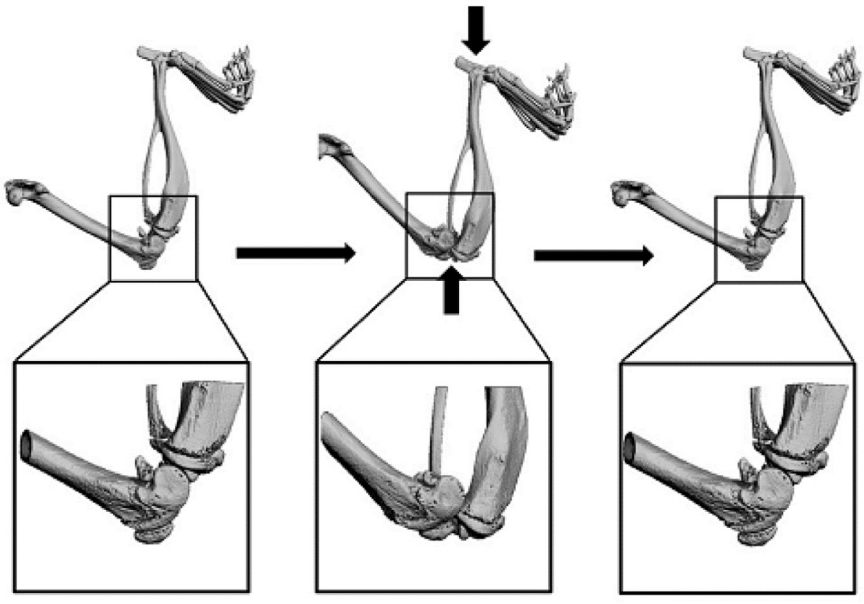

Fig. 1. Tibial compression overload model.