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Review

Age-related changes in the knee meniscus

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ABSTRACT

Background: Aging is the most prominent risk factor for the development of osteoarthritis (OA), which affects knees and causes major health burdens. Meniscal dysfunction mostly based on degeneration contributes to the development and progression of knee OA. Meniscal degeneration is caused by various extrinsic factors, such as repetitive trauma or leg malalignment, while meniscal aging is considered as internal changes, such as molecular or cellular changes. Little is known about age-related changes in the meniscus. Therefore, this review aimed to summarize and clarify the understanding of the aged meniscus.
Methods: There are few articles about natural aging in the meniscus, because most reports only demonstrate the effects of OA on the meniscus. We searched PubMed (1948 to November 2016) to identify and summarize all English-language articles evaluating natural aging in the meniscus.
Results: There is evidence of compositional change in the meniscus with aging, involving cells, collagens, and proteoglycans. In addition, as recent reports on the natural aging of cartilage have indicated, senescence of the meniscal cells may also lead to disruption of meniscal cells and tissue homeostasis. Due to the low turnover rate of collagen, accumulation of advanced glycation end-products largely contributes to tissue stiffness and vulnerability, and finally results in degenerative changes or tears. Furthermore, environmental factors such as joint fluid secreted by inflamed synovium could also contribute to meniscal tissue deterioration.
Conclusions: Age-related changes induce meniscal tissue vulnerability and finally lead to meniscal dysfunction.

Contents

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1. Introduction

Aging is an inevitable process, and is associated with functional impairment of various organs and tissues, including the musculoskeletal system in the form of osteoarthritis (OA), osteoporosis, and sarcopenia, age-related deterioration of joints, bones, and muscles, respectively [1]. Equally, degeneration is often used as almost the same meaning as aging. However, aging can be considered separately from degeneration because degeneration can even occur in the young. In fact, although it has already been noted that degeneration is difficult to separate from aging [2,3], it has become acceptable to distinguish aging from degeneration in the case of articular cartilage and intervertebral discs [4–6]. Degeneration is defined as the structural and functional failure of the tissue, while aging is defined as a result of time-dependent accumulation of molecular and cellular damage. Knee meniscus also changes with aging, but little is known about meniscal changes with aging, not with degeneration. Cellular aging (also referred to as cellular senescence) and tissue aging have recently gained much attention [7], and aging research has begun to focus on basic biological processes. It is of critical importance to understand how molecular and cellular changes occur in the aged meniscus.

Clinically, meniscal dysfunction is mostly caused by tear based on degeneration, such as a horizontal tear or a posterior root tear [8–10]. Knee OA causes a major problem in the most fundamental daily activities, such as walking and running. Thus, preventing its pathogenesis and progression is vital for maintaining knee functions in old age [11–14]. Not all knee OA is caused by the aging process, as meniscal injury can induce knee OA even in the young. However, the age-related changes might greatly contribute to its pathogenesis as in the cartilage [15].

This review aimed to update the current knowledge associated with the aged meniscus. This might lead to methods to slow the progression of meniscal degeneration or to the development of a novel strategy for treatment.

2. Normal meniscus: structure and composition

The knee joint contains two crescent-shaped menisci between the femoral condyles and the tibial plateau. They are peripherally thick and taper centrally to a thin margin. The medial meniscus covers 50–60% of the medial tibial plateau, and the lateral meniscus covers 70–80% of the lateral plateau [16]. Both menisci have anterior and posterior tibial attachments.

Although the fetal meniscus is fully vascularized [17], there is a gradual decrease in vascularity during development. By the age of 10 years, only the peripheral 10–30% of the meniscus is vascularized [17,18], and the remaining inner region is avascular. Three regions of the meniscus are classified: the outer red–red zone, the middle red–white zone, and the inner white–white zone.

The meniscus is mainly composed of water (72%) with the remainder being extracellular matrix (ECM) and cells [19]. The dry weight is composed of 70% collagen, followed by 17% proteoglycans, two percent Deoxyribonucleic acid (DNA), one percent adhesion glycoproteins, and eight percent non-collagenous proteins, including one percent elastin [19–22]. Type I accounts for the majority of the collagen, with variable amounts of types II, III, V, and VI [21,22]. Type I collagen fibers are predominantly oriented circumferentially; this fiber arrangement serves to transfer vertical compressive load into hoop stresses. Radially oriented collagen 'tie' fibers are also present and woven between the circumferential fibers to create a fibrillary network. The amount of proteoglycans in the meniscus is one-eighth that present in the articular cartilage [23], and regional variation has also been observed [24]. Proteoglycans are the major component of ECM. The main types of glycosaminoglycans (GAGs) are chondroitin-6-sulfate (40–60%), dermatan sulfate (20–30%), chondroitin-4-sulfate (10–20%), and keratin sulfate (15%) [19,25]. Adhesive glycoproteins that bind with other matrix or cells are present within the meniscus; these include type VI collagen, fibronectin, and thrombospondin [21].

Three types of meniscal cells are classified according to their shape and localization. The outer zone cells have a fusiform shape and are described as fibroblasts, while the inner zone cells have more rounded shape and are described as chondrocytic cells [26]. A third cell population has a flattened and fusiform appearance, and localizes in the superficial zone, and is a progenitor population [27,28]. Although the inner chondrocytic cells are similar to articular chondrocytes, meniscal chondrocytic cells produce type I collagen. Thus, these inner cells are called fibrochondrocytes and are derived from another origin [29].

These material compositions of the meniscus are closely related to its unique functions, such as joint stabilization, load transmission, shock absorption, and lubrication. The decline in the quality of each property with molecular or cellular damage may be the cause of aging of the meniscus.

3. Changes with advancing age

3.1. Macroscopic appearance

Macroscopically, the aged meniscus appears more opaque, with dark yellowish color, compared to the healthy young meniscus, which has a translucent, smooth, and glistening surface [30] (Figure 1). Aged hyaline cartilage and aged vertebral disc nucleus are

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