Review article

Effects of aging and physical activity on articular cartilage: a literature review

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Abstract

The overall aim of this literature review is, by making use of major databases, to introduce the concepts about the articular cartilage structure and the effects of aging on articular cartilage. The effects of physical exercises on those cartilages are also discussed. The most important observations found are: cartilage thickness decreases gradually with age as well the content of proteoglycans and water, and there is an increase and the collagen fibrils, which may be associated with the increased rigidity and fragility of the articular cartilage. When properly done, physical activities produce compressive stimuli which enhance the activity of chondrocytes increasing its nuclear volume density per area, as well as the width of the layers leading to greater resistance to compression. Another consequence is extracellular matrix hydration resulting in greater mechanical resistance and elasticity and a consequent increase the number of collagen fibrils which generates greater resistance to deformation and implies less rigidity. These facts reduce the risk of breakdown of cartilage when it is subjected to high mechanical demand.

Keywords: articular cartilage, exercise.

1 Introduction

Articular cartilage is a connective tissue that covers the articulating surfaces of bones within synovial joints. Its primary function is to absorb the mechanical shock and distribute the weight having a minimum coefficient of friction (LEVANON and STEIN, 1991; HARDINGHAM, FOSANG and DUDHIA, 1992; HEISE and TOLEDO, 1993; TRATTNIG, 1997; ALBERTS, BRAY, LEWIS et al., 1999; HUBER, TRATTNIG and LINTNER, 2000). Articular cartilage is composed of two different elements: cells called chondrocytes and an extracellular matrix (BURSTEIN, BASHIR and GRAY, 2000).

Chondrocytes regulate the metabolism of extracellular matrix through mechanical, physicochemical, and electrical stimuli (TRATTNIG, 1997; POOLE, KOJIMA, YASUDA et al., 2001) whose intensity modulates cellular responses (SMITH, LIN, TRINDADE et al., 2000).

The extracellular matrix is composed of a network of collagen fibrils, water, and large amounts of proteoglycans (HARDINGHAM, FOSANG and DUDHIA, 1992, VOGEL, 1994; TRATTNIG, 1997; HUBER, TRATTNIG and LINTNER, 2000). Proteoglycans (PGs) are molecules that are made up of a core protein attached to glycosaminoglycan (GAG) chains (HASCALL and HASCALL, 1981; HASCALL and KIMURA, 1982; VAN KUPPEVELT, DOMEN, CREMERS et al., 1984; WIGHT, HEINEGARD and HASCALL, 1991; RUOSLAHTI and YAMAGUCHI, 1991; YANAGISHITA, 1993; BRANDAN, 1994, NISHIMURA, HATTORI, and TAKAHASHI, 1996; MICHELACCI, 1996, HUBER, TRATTNIG and LINTNER, 2000; GOMES, 2001).

Aggrecan is the main PG in the articular cartilage composed of the following GAGs: chondroitin, sulfate, and keratan sulfate (HASCALL and HASCALL, 1981; CARNEY and MUIR, 1988; GOMES, 2001). The interaction between aggrecan and hyaluronic acid is responsible for retaining water in the cartilage (CARNEY and MUIR, 1988). The interaction between collagen fibrils and aggrecan makes the extracellular matrix of cartilage highly hydrophilic, which leads to high resistance to compressive mechanical loads in addition to regulating the movement of molecules in the extracellular medium (MAROUDAS, 1976; PALMOSKI, COLYER and BRANDT, 1981; MUIR, 1983, O'CONNOR, ORFORD, and GARDNER, 1988; WIGHT, HEINEGARD and HASCALL, 1991; HARDINGHAM, MUIR, KWAN et al., 1987; SÄÄMÄMEN, KIVIRANTA, JURVELIN et al., 1994; ALBERTS, BRAY, LEWIS et al., 1999; CULAV, CLARK and MERRILEES, 1999; HUBER, TRATTNIG and LINTNER, 2000).

Collagen, together with the PGs, is also responsible for resisting the deformations to which the cartilage is subjected (ROUGHLEY and WHITE, 1980; SCHMIDT, MOW, CHUN et al., 1990). During the aging process, there are changes in the structure of the extracellular matrix (ROUGHLEY, 2001) resulting in a tissue with reduced ability to absorb mechanical stress (LOESER, 2000; HULDELMAIER, GLASER, ENGLMEIER et al., 2001) and more susceptible to degenerative diseases.

Osteoarthritis is a degenerative joint disease, which is associated with aging and mainly affects the articular cartilage. It is one of the most common causes of pain, disability, and decreased quality of life among middle-aged and older adults (ATRA, 1995; NEWTON, MOW, GARDNER et al., 1997). Excessive loading, anatomical abnormalities, injuries, repetitive use, and decreased weight bearing in the joint are triggers of this disease (KIVIRANTA, JURVELIN, TAMMI et al., 1987; AROKOSKI, KIVIRANTA, JURVELIN et al., 1993; WALKER, 1996; NEWTON, MOW, GARDNER et al., 1997; JORTIKKA, INKINEN and TAMMI, 1997). However, it is worth mentioning that osteoarthritis is not necessarily caused only by aging itself (NEWTON, MOW, GARDNER et al., 1997).

Numerous studies have focused on the prevention of osteoarthritis in the elderly, especially because the incidence of osteoarthritis is expected to increases in the coming decades causing social and economic problems (WALKER, 1996). One way to avoid or minimize the effects of osteoarthritis is through appropriate physical activities.

Several studies have been conducted to indentify the influence of different types of physical activities that can minimize the deleterious effects of aging on articular cartilage (DEGROOT, VERZIJL, BANK et al., 1999; JONES, GLISSON, HYNES et al., 2000; HULDELMAIER, GLASER, ENGLMEIER et al., 2001; AROKOSKI, KIVIRANTA, JURVELIN et al., 1993; BUCKWALTER, 1995; PAP, EBERHARDT, STÜRMER et al., 1998; HÄÄPALA, AROKOSKI, HYTTINEN et al., 1999). The purpose of the literature review conducted is to describe and compare the results of studies on the effects of aging and various types of physical exercises on the articular cartilage in order to ascertain their applicability to improve health and quality of life for seniors.

2 Material and methods

PubMed (www.pubmed.nl) and MEDLINE databases were used to the conduct a literature search using keywords without restrictions. In this systematization, papers were searched using the following Keywords: aging, articular cartilage, exercise.

3 Results

3.1 Structure of articular cartilage

Biochemically, approximately 70% of the articular cartilage is composed of water and 30% of solids, of which 5-6% are inorganic components (mainly hydroxyapatite), and the remaining 25% are organic compounds. Type II collagen constitutes approximately 68% of the organic components, and the remaining 22% is formed by proteoglycan (KÄÄB, GWYN and NÖTZLI, 1998; TRATTNIG, 1997; HUBER, TRATTNIG and LINTNER, 2000; BURSTEIN, BASHIR and GRAY, 2000; MATYAS, HUANG, CHUNG et al., 2002). All components of the matrix are continuously remodeled by the cartilage cells, chondrocytes (WU and HERZOG, 2002).

Articular cartilage has three layers: the uppermost superficial layer, with collagen fibrils aligned parallel to the articular surface, which favors the distribution of pressure; the middle layer with collagen fibrils oriented perpendicular to the articular surface; and the deep layer, also with collagen fibrils running perpendicular to the articular surface. The arrangement of collagen fibrils in the middle and deep layers suggests great shock absorbing ability (WALDSCHMIDT, RILLING, KAJDACSY-BALLA et al., 1997; WU and HERZOG, 2002). The chondrocytes are embedded in the matrix in all layers.

Collagen fibrils are composed of protein macromolecules and provide articular cartilage with resistance to tension (BURSTEIN, BASHIR and GRAY, 2000). Collagen type II constitutes 85% the total collagen content of the total of articular cartilage, and collagen types VI, IX, and XI constitute the remaining 15% (RIVERO, TEODORO, VELOSA et al., 2000), which are essential for the survival of chondrocytes (KIM, SUH and SONG, 2001).

PGs are macromolecules of high molecular weight that consist of a protein covalently attached to one or more glycosaminoglycan (GAG) side chains (HUBER, TRATTNIG and LINTNER, 2000; GOMES, 2001), which are sulfated carbohydrate chains (MICHELLACCI, 1996; STEVENS and LOWE, 1997). Aggrecan is the main PG in articular cartilage and is covalently attached to chondroitin sulfate and keratan sulfate chains between the collagen fibrils linked with hyaluronic acid. It presents resistance to loads with minimal deformation (GOMES, 2001; CHAMBERS, COX, CHONG et al., 2001).

The main GAGs found in mammals are chondroitin-4-sulfate, chondroitin-6-sulfate, dermatan sulfate, keratan sulfate, heparan sulfate, heparin, and hyaluronic acid (RUOSLAHTI and YAMAGUCHI, 1997; STEVENS and LOWE, 1997).

Chondrocytes regulate the metabolism of extracellular matrix by mechanical, physicochemical and electrical stimuli (TRATTNIG, 1997; POOLE, KOJIMA, YASUDA et al., 2001), whose intensity modulate the responses of cellular functions (SMITH, LIN, TRINDADE et al., 2000).

Removing any of the biological components of articular cartilage can cause damage to it (VASSAN, 1983), movement and weight bearing ensure the functionality of the cartilage and maintain its cellular properties and mechanical behavior (O'CONNOR, ORFORD, and GARDNER, 1988; BEAUPRÉ, STEVENS, and CARTER, 2000).

3.2 Effects of aging

The synthetic activity of chondrocytes in all articular cartilage layers declines with age (KARVONEN, NEGENDANK, TEITGE et al., 1994). This decline is essential for maintaining the structure of the extracellular matrix and leads to a gradual decrease in its thickness (KARVONEN, NEGENDANK, TEITGE et al., 1994; HULDELMAIER, GLASER, ENGLMEIER et al., 2001). These variations in the synthesis of cells, which are aging-programmed and beneficial, occur throughout life, and their purpose is to adapt the articular cartilage to mechanical and chemical needs of the individuals from the fetal period up to longevity (ROUGHLEY, 2001).

The decline in cellular activity in all articular cartilage layers can be associated with a decrease in the growth factor (LOESER, 2000; ROUGHLEY, 2001; and apoptosis ADAMS and HORTON, 1998), intensified at older age (KARVONEN, NEGENDANK, TEITGE et al., 1994). It is important to mention that there are variations in the level of age-related cartilage degradation, which sets precedents for histopathologic degeneration (PLAAS, WONG-PALMS and ROUGHLEY, 1997; ROUGHLEY, 2001; CHAMBERS, COX, CHONG et al., 2001).

Age also produces considerable changes in extracellular matrix components, especially in the amount and structure of PGs (PLAAS, WONG-PALMS and ROUGHLEY, 1997;

ROUGHLEY, 2001). The major mechanical unloading areas of the articular cartilage undergo an increase in roughness with increasing age (LOESER, 2000) since the content and size of the subunits of PGs (ROUGHLEY and WHITE, 1980), as well as their synthesis and water content (DEGROOT, VERZIJL, BANK et al., 1999), are reduced. Thus, both the hyaluronic acid molecule and the aggrecan molecule reduce in size with age due to proteolytic modifications in the main chain. There is a reduction in the amount of GAG bound to aggrecan, which explains the decrease in the hydration of articular cartilage (LOESER, 2000) and its lower ability to respond to mechanical loading Loeser (2000), Huldelmaier, Glaser, Englmeier et al. (2001).

Aging and a sedentary lifestyle conspire to reduce mechanical stimulus, which in turn decreases the synthesis of PGs in articular cartilage (DEGROOT, VERZIJL, BANK et al., 1999). In addition, the ability to repair damaged matrix is reduced (LOESER, 2000; ROUGHLEY, 2001).

With respect to the collagen network of cartilage, there is an increase in the number of bonds between collagen fibrils (LOESER, 2000), which is possibly associated with increased stiffness and brittleness of the articular cartilage with aging (BANK, BAYLISS, LAFEBER et al., 1998).

All of these age-related changes that occur in the cartilage increase the risk of cartilage damage, but they do not necessarily lead to osteoarthritis (KARVONEN, NEGENDANK, TEITGE et al., 1994) because the cell synthesis is generally able to maintain the morphofunctional integrity of cartilage (ADAMS and HORTON, 1998; HULDELMAIER, GLASER, ENGLMEIER et al., 2001).

3.3 Effects of exercises

Several studies have shown that the application of constant compressive loading is important to maintain the normal structure of articular cartilage (KIM, SAN, GRODZINSKY et al., 1994; BUCKWALTER, 1995; MATYAS, HUANG, CHUNG et al., 2002).

It has already been proved that regular moderate physical activity leads to improvements in the biomechanical and biological properties of articular cartilage (KIVIRANTA, TAMMI, JURVELIN et al., 1988) by acting as a chondroprotective (OTTERNESS, ESKRA, BLIVEN et al., 1998) increasing the synthesis and concentration of PGs and GAGs (KIVIRANTA, JURVELIN, TAMMI et al., 1987; KIVIRANTA, TAMMI, JURVELIN et al., 1988; LAMMI, HÄKKINEN, PARKKINEN et al., 1993; VAN DEN HOOGEN, VAN DE LEST, VAN WEEREN et al., 1998) and the other components of cartilage matrix (VISSER, VAKAMOEN, DEKONING et al., 1994; EGRI, BATTISTELLA and YOSHINARI, 1999). It also increases cartilage thickness (LAMMI, HÄKKINEN, PARKKINEN et al., 1993; ESPANHA, LAMMI, HYTTINEN et al., 2001).

Kiviranta, Tammi, Jurvelin et al. (1992); Lane and Buckwalter (1993), Visser, Koning, Lammi et al. (1998) observed changes in the articular cartilage with progressive exercises in young adult animals. They noted an increase in the concentration and thickness of PGs without changes in its integrity. Subjects of various ages without joint pathology showed tolerance to prolonged physical training without adverse effects and no acceleration in the development of the degenerative joint disease (BUCKWALTER, 1995).

With regard to immobilization, its duration and the amount of weight bearing on the resumption of mobilization are important to determine the response of articular cartilage. According to Hääpala, Arokoski, Hyttinen et al. (1999), the loss of GAGs in the uppermost superficial layer of articular cartilage in young adult animals does not alter the physiological compressive strength of this material during physical exercises after immobilization.

Exercises that excessively compress the articular cartilage may bring adverse effects by increasing the internal flow of water leading to the disruption of the matrix and susceptibility to degenerative changes (SAH, GRODZINSKY, PLASS et al., 1992; BUCKWALTER, 1995) in addition to the reduction of their PGs in young adult animals (AROKOSKI, KIVIRANTA, JURVELIN et al., 1993).

A positive response of articular cartilage is mainly associated to a large extent with the intensity and frequency of compressive stimuli inducing increased activity of chondrocytes, which is identified by its increased nuclear volume density per area and thickness of the layers, which leads to greater resistance to compression. Another consequence is extracellular matrix hydration resulting in greater mechanical resistance and elasticity and a consequent increase in the number of collagen fibrils which generates greater resistance to deformation and implies less rigidity. These facts reduce the risk of breakdown of cartilage when it is subjected to high mechanical demand.

4 Discussion

The appreciation of physical activity as a significant health factor in improvement of quality of life and to promote health has been growing rapidly in recent years, particularly among people aging. This is due to the fact that there are many well-known beneficial effects of exercises on the body. This study also focused on taking those effects on articular cartilage into consideration, especially in older age groups in which there is increased incidence of diseases such as osteoarthritis. It is known that osteoarthritis is a disease of the musculoskeletal system associated with a sedentary lifestyle.

These statements were corroborated by a similar study that reported a thinning of articular cartilage in aging animals (KARVONEN, NEGENDANK, TEITGE et al., 1994; HULDELMAIER, GLASER, ENGLMEIER et al., 2001) suggesting that this fact occurs due to the decrease in cell activity over time.

Since osteoarthritis is associated with aging, increasing life expectancy is a global trend, and urban populations lead a more sedentary lifestyle, it can be said that osteoarthritis can affect large segments of the population influencing the cost of health services and quality of life.

Regular physical exercises is an alternative to reverse this situation since in physical activities with high compressive unloading on intra-articular structures, such as running (VASSAN, 1983; BIHARI-VARGA, FRAKAS and BIRÓ, 1984; VISSER, VAKAMOEN, DEKONING et al., 1994; OTTERNESS, ESKRA, BLIVEN et al., 1998; PAP, EBERHARDT, STÜRMER et al., 1998; EGRI, BATTISTELLA and YOSHINARI, 1999), there is an increase in the synthetic activity of chondrocytes.

These results are consistent with previous studies that show that there is a large number of aggrecan molecules in areas of higher compressive unloading on weight-bearing joints, such as those conducted by Wight, Heinegard and Hascall (1991), Hardingham, Fosang and Dudhia (1992), Yanagishita (1993) and Chambers, Cox, Chong et al. (2001).

In some types of physical activities in which there is total or partial support in the middle of the body, such as swimming, there is less impact and overload on intra-articular structures (HARRINSON, HILLMAN and BULSTRODE, 1992; DOWZER, REILLY and CABLE, 1998). In these types of exercises, great part of the overload is dissipated throughout the limb muscles keeping the joints in constant motion, with no specific points of weight bearing, unlike what occurs during physical activities under gravitational action (KÄÄB, GWYN and NÖTZLI, 1998).

It is assumed that the intra-articular overload generated by this type of physical activity is mild to moderate and thus insufficient to increase chondrocytes metabolism and change the thickness of articular cartilage (PALMOSKI, COLYER and BRANDT, 1980; KIVIRANTA, JURVELIN, TAMMI et al., 1987; HARRINSON, HILLMAN and BULSTRODE, 1992; AROKOSKI, KIVIRANTA, JURVELIN et al., 1993; VISSER, VAKAMOEN, DEKONING et al., 1994; VAN DEN HOOGEN, VAN DE LEST, VAN WEEREN et al., 1998; BEAUPRÉ, STEVENS and CARTER, 2000; CHIARELLO, 2003).

However, either in water or on the ground, where there is no decline in the influence of gravitational action such as in walking, physical activities that unload mild to moderate compression on intra-articular structures regulate the balance of extracellular matrix remodeling, which is in agreement with Palmoski, Colyer and Brandt (1980), Arokoski, Kiviranta, Jurvelin et al. (1993), Visser, Vakamoen, Dekoning et al. (1994), Karvonen, Negendank, Teitge et al. (1994), Waldschmidt, Rilling, Kajdacsy-Balla et al. (1997), O'connor, Orford, and Gardner (1988), van den Hoogen, van de Lest, van Weeren et al., 1998, Beaupré, Stevens, and Carter (2000), Wu and Herzog (2002) and Chiarello (2003).

According to the studies of Skinner and Thomson (1985a, b), Harrinson, Hillman and Bulstrode (1992), Becker and Cole (1997), Campion (1998) and Fitzgerald, Childs, Ridge et al. (2002), activities that reduce stress on weight bearing joints do not increase articular cartilage thickness, but they indeed preserve this tissue.

5 Conclusion

Mild or moderate physical activities, such as hiking and swimming, or a water activity of similar limb support have the ability to maintain the integrity of articular cartilage, either in terms of thickness or the increase in the volume of the chondrocyte's nuclear volume density per unit area.

High intensity physical activities, such as running, promote considerable increase in the synthetic activity of chondrocytes, as observed by the thickness of all articular cartilage layers, by the increased nuclear volume density per area of chondrocytes.

Regular light and moderate physical activities, such as walking and swimming, and intense activities, such as running, are habits that can prevent or delay the onset of osteoarthritis, which may contribute to the reduction of public health costs and to the maintenance and improvement and of quality of life.

Further in vivo experiments with humans are necessary since nearly all the studies reviewed were based on animal models. Therefore, the findings may not apply to an adequate prescription of physical training loads for humans, as well as determining the optimum frequency in terms of volume, intensity, or programming macro, meso, and microcycles training sessions.

It is known that strength physical activities, such as weight training, are essential to increase the shock absorption by the musculoskeletal system, as well as to stabilize the joints and allow proper implementation of cyclic or acyclic aerobic activities. This issue also deserves further in vivo investigation in humans, especially on aging, considering articular cartilage.

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