THE EFFECT OF DIFFERENT IMPACT EXERCISE TRAINING ON DEFORMATIONAL BEHAVIOR AND FUNCTIONAL ADAPTATION OF ARTICULAR CARTILAGE

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ABSTRACT

THE EFFECT OF DIFFERENT IMPACT EXERCISE TRAINING ON DEFORMATIONAL BEHAVIOR AND FUNCTIONAL ADAPTATION OF ARTICULAR CARTILAGE

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The objective of the present study was to investigate deformational behavior and functional adaptation of articular cartilage by comparing the changes of biochemical osteoarthritis markers' concentrations due to 30-min exercise after 12-weeks of regular high impact, impact or non-impact exercise.

Blood samples were drawn from 44 healthy sedentary males immediately before, immediately after and 0.5 h after a 30-min moderate walking exercise. Osteoarthritis biomarkers' (Serum COMP and CTX-I) concentrations were determined with enzyme-linked immunosorbent assay. After the first measurements, participants were randomly assigned to running, cycling, swimming, and control groups. All groups except for control group trained for 12 weeks. After 12-weeks, post tests were applied.

Multivariate tests indicated a significant fatigue and resting effect on serum COMP concentration in all groups at pre- and post-tests. Therefore, pair wise comparisons were conducted in order to assess the differences across all groups and conditions. Results indicated significant differences in post-test measurements among phases of groups except for running group. However, fatigue or resting did not change the concentration of serum CTX-I in any groups during the tests.

According to results, moderate walking activity has an influence on the increase of serum COMP concentrations of young sedentary men. However, 12 weeks regular weight-bearing high impact physical exercise decreases the deformational effect of walking activity by functional adaptation of articular cartilage to specific environmental requirements.

Key words: COMP, CTX-I, Running, Cycling, Swimming.

ÖZ

FARKLI DARBELERDEKİ EGZERSİZLERİN EKLEM KIKIRDAĞININ DEFORMASYONEL DAVRANIŞINA VE FONKSİYONEL ADAPTASYONUNA ETKİSİ

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Bu çalışmanın amacı, 12 hafta süreyle yapılan darbeli, yüksek darbeli veya darbesiz egzersizlerden sonra, 30 dakikalık egzersizin eklem kıkırdağında sebep olduğu deformasyonel davranışı ve fonksiyonel adaptasyonu, serum osteoartrit işaretleyicilerinin konsantrasyonundaki değişikliği değerlendirerek araştırmaktı.

Kan örnekleri, 44 sağlıklı sedanter erkekten 30 dakikalık orta şiddette yürüme egzersizinden hemen önce, hemen sonra ve yarım saat sonra alındı. Osteartrit biyo-işaretleyicilerinin (Serum KOMP ve CTX-I) konsantrasyonu ELIZA yöntemi ile belirlendi. İlk ölçümlerin ardından katılımcılar rasgele örneklem metodu ile koşu, bisiklet, yüzme ve kontrol gruplarına ayrıldı. Kontrol grubu haricinde tüm gruplar 12 hafta boyunca antrenman yaptı. 12 hafta sonunda, son testler uygulandı.

Çokdeğişkenli testler tüm gruplarda ilk ve son testlerde yorgunluğun ve dinlenmenin serum KOMP konsantrasyonu üzerinde anlamlı bir etkisi olduğunu gösterdi. Bu nedenle, hangi grupların ortalamasının değiştiğini değerlendirmek için ikili karşılaştırmalar uygulandı. Koşu grubu hariç diğer grupların son test ölçümlerindeki fazlarda da anlamlı farklar olduğu ortaya çıktı. Ancak testler sırasında yorgunluk ve dinlenme serum CTX-I konsantrasyonunu değiştirmedi.

Sonuçlara göre, orta şiddetli yürüme aktivitesi genç sedanter erkeklerin serum KOMP konsantrasyonunu yükseltebilecek etkiye sahiptir. Ancak, 12 hafta süreyle düzenli olarak yapılan, vücudunun ağırlığının taşındığı ve yüksek çarpma etkisi yaratan egzersizler, eklem kıkırdağının belirli çevresel gereksinimlere fonksiyonel adaptasyonu sayesinde yürüme aktivitesinin sebep olduğu deformasyonel etkiyi düşürmektedir.

Anahtar Kelimeler: KOMP, CTX-I, Koşu, Bisiklet, Yüzme

To Göşeğağ, Aslan & Sırma
For their unconditional love

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CHAPTER 1

INTRODUCTION

1.1 Background of the Study

About 140 years ago famous biologist Charles Darwin (1872) stated that the ability of tissues to emerge and maintain their structure in accordance with specific environmental requirements has been called "Functional Adaptation" (Darwin, as cited in Eckstein, Hudelmaier, & Putz, 2006). Processes of functional adaptation have been regarded as occurring during the development of the central nervous system (e.g. the visual cortex), internal organs (e.g. the kidney) and in tissues with primarily mechanical functions, such as muscle and bone (Eckstein, et al., 2006).

Today almost all the principles of physiological conditioning and sports training theories are based on functional adaptation. According to ACSM's guidelines (2001) there are numerous effects of regular physical activity that can be called as functional adaptation such as improvement in cardiovascular and respiratory functions, reduction in coronary artery disease risk factors, control of hypertension, decrease of obesity, and descent of cancer risk. Moreover, effect of regular exercise is most obvious in muscle and bone. A muscle hypertrophy elicited by using moderate loads, high volume and short to moderate rest periods at training (Baechle & Earle, 2000). In addition, in a twin study, it is revealed that some part of the variability of the peak bone mineral content and density are determined by genotype, but other part is determined by life style and epigenetic factors, such as exercise, diet (Pocock et al., 1987). On the other hand, prolonged skeletal unloading in long-duration spaceflight has shown consistent loss of bone mineral, especially at the lower skeleton (Lang, 2006; LeBlanc, Spector, Evans & Sibonga1, 2007). These findings are evidence of well defined mechanism of functional adaptation of muscle and bone to mechanical load.

Cartilage tissue has also mechanical function like bone or muscle tissues. Physical forces are known to influence the synthesis, assembly and degradation of the cartilage extracellular matrix (Giannoni, Siegrist, Hunziker & Wong, 2003). Cyclic loading is the most common mode of loading in human lower limb joint. These joints are subjected on average to between 1 and 4 million load cycles per year (Barker & Seedhom, 1997; Seedhom & Wallbridge, 1985). However, the functional adaptations of a cartilage tissue especially to physical exercises were the subjects that had not been searched for enough. Up to now, the effect of exercise on articular cartilage tissue has traditionally been examined in animal models (Lammi et al., 1993), and until recent times there have been limited researches about the relation between human cartilage and exercise.

There is no exact combination of sport exercise that will be beneficial for cartilage health and preventive precautions. Moreover, there are some exercise recommendations for arthritis treatment and rehabilitation (Gordon, 1993; Zhang et. al, 2008). In these recommendations patients were encouraged to undertake regular aerobic, muscle strengthening and range of motion exercises. Also, there are many recommendations about exercises for general health (ACSM, 2001; Cavill, Kahlmeier & Racioppi, 2006). Swimming, cycling and running are some of the most recommended aerobic exercise types for both arthritis and general health in literature. These three sport kinds are also relatively most accessible and common sports all over the world.

According to Austin and Noble (1994), swimming is the best kind of exercise which is beneficial for all the systems and functions. Swimming incorporates both the upper and lower body musculature. Since it is a nonweight-bearing activity, the chances of exacerbating arthritis are extremely low (Gordon, 1993). Evidence for pain relief and improvements in stiffness in patients with symptomatic hip osteoarthritis following exercise in water was also reported by Cochrane, Davey & Edwards (2005). In addition to benefits of swimming on arthritis cases, Katz & Bruning (1993) claimed that enough swimming helps improving circulatory and respiratory functions, gives stronger and firmer muscles, increases flexibility, helps losing weight, aids physical therapy and has many other benefits. Maglischo & Brennan (1985) also listed the benefits of swimming as appearance benefits, other muscular and skeletal changes, improved flexibility, circulatory benefits, respiratory benefits, psychological benefits.

Cycling is another exercise type which is commonly recommended for treatment of arthritis and general health. Cycling has become a favorite recreational sport all over the world. The total number of cyclist who exercises regularly in US is estimated as more than 50 million by the Bicycle Institution of America (Carmichael and Burke, 1994). And one of the most popular home equipment exercise item is a stationary bicycle; more than three million are bought every year (Carmichael and Burke, 1994). Both kinds of cycling have similar benefits but in road cycling, roads tend to go up and down unexpectedly. Also an additional mild joint stress by outdoor cycling on shoulder, elbow and wrist might occur (Gordon, 1993). Therefore, stationary bicycle is preferable in some cases. Carmichael and Burke (1994) listed the benefits of cycling as cardiovascular fitness benefits improved flexibility, improved body composition and improved muscular endurance and strength.

In literature there are lots of sources explaining the similar benefits of running on general health like swimming and cycling. In the report of surgeon general, running is one of the most pronounced physical exercise types. Especially long-distance running is currently one of the most popular fitness activities, involving an estimated 30 million people in the United States alone (Hofmann,Wortler & Imhoff, 2004). Also, according to Anderson and his collaborates (2006) Running and jogging, like walking, is one of the best aerobic activities. They states that running is just extension of walking, and will add intensity for physical activity and also takes less time for the same aerobic and calorie-burning benefits. One another advantage of running is that bones and joints get more pressure exerted on during running therefore, they grow stronger and this affords better protection against osteoporosis (Anderson et. al., 2006). Also, running is a easy way for most people to get regular exercise because it doesn’t require special facilities or equipment except for a proper shoe.

As a result all these three exercises are almost most common and recommended exercises. The effect of different exercises, durations, intensities and densities on general health studied extensively in the literature. And as a general expectation a well-organized exercise program, with these kinds of exercises, is the most beneficial instruction to achieve the sense of well-being. On the other hand, the effect of recommended exercise interventions on the articular cartilage is not clear enough. Previous studies limited with the animal and cadaveric studies or injured or elite athletes evaluations. But in the designing of the present study we examined the effect of most recommended exercise interventions on articular cartilage of knee joint.

1.2 Rationale of the Study

As a mechanical tissue, mechanosensitivity of cartilage tissue has not been investigated extensively unlike bone or muscle. Main reason of this was the lack of non-invasive methods that allow human articular cartilage to be studied directly in vivo. However, with quantitative magnetic resonance imaging and validated biochemical joint damage markers, investigations on these topics have become popular (Eckstein, Hudelmaier, Putz, 2006; Garnero et al., 2002; de Jong et al., 2008).

Preliminary researches about the effect of exercise on articular cartilage were generally on animal models (Lammi et al, 1993). Recent researches tested effect of physical exercise on human articular cartilage. In this researches investigators generally, compared structure of elite athletes' articular cartilage with those of non-athletes (Eckstein et al, 2002; Muhlbauer et al, 2000) or effect of one bout of training on articular cartilage (Kersting, Stubendorff, Schmidt & Bruggemann, 2005; Mundermann, Dyrby, Andriacchi & King 2005). However, results of these researches are not enough to conclude longitudinal adaptation or deformation of articular cartilage due to physical exercise. Also evidence of the effect of different exercise on articular cartilage is still unclear.

Therefore, this study would explain the short term (deformational behavior) and long term (functional adaptation) changes of articular cartilage of healthy non-athlete men due to regular exercise. Another important role of this study would be to determine which type of physical exercise could be better or not for knee cartilage. If alterations in articular cartilage are evident in any type of exercise after 12 weeks regular exercise, then further studies investigating the effect of different quantity and quality of exercise could be worthwhile.

1.3 Research Questions

Does 12-weeks of high, medium and low impact exercises effect the (a) deformational behavior (b) functional adaptation of human articular cartilage?

1.4 Purpose of the Study

The purpose of this study was to compare changes of biochemical markers of cartilage degradation levels during a 30-min exercise after 12-weeks of regular high, medium or non impact exercises.

1.5 Research Hypotheses

1. There will be no significant difference in deformational behavior of the knee cartilage due to 12-week

    High-impact (running) exercise

    Medium-impact (cycling) exercise

    Low-impact (swimming) exercise

2. There will be no significant difference in functional adaptation of the knee cartilage due to 12-week

   High-impact (running) exercise

   Medium-impact (cycling) exercise

   Low-impact (swimming) exercise

1.6 Delimitations

1. Participants consisted of 18-25 years old male non-athletes.
2. Volume of the exercises was the same for all experimental groups.
3. Intensity of the exercises was the same for all experimental groups.
4. Participants who had sustained previous lower extremity injuries were excluded from the study.
5. All measurements were performed using the same set-up throughout the course of testing for all participants.

1.7 Limitations

1. Participants of this study were not selected randomly.
2. Participants were limited to those students taking General Physical Conditioning course as an elective course
3. Participant group was composed of only male subjects.
4. Morphological changes of articular cartilage were not observed.
5. Cycling and running exercises were performed on stationary ergometer and treadmill.
6. Daily activities of the participants were not controlled.
7. Interaction between groups was not controlled

1.8 Assumptions

1. The participants participated the tests at fully recovered state
2. The participants gave their best effort during performance tests
3. The participants of experimental groups did not participate in any extra physical exercises during intervention period
4. The participants of control group did not participate any physical exercise during intervention period

1.9 Definition and Abbreviation of Terms

The following are definitions of terms that were operationally defined throughout this study.

Maximal oxygen consumption (VO_2max): The maximum amount of oxygen that can be consumed per minute during maximal exercise; also known as aerobic power and maximal oxygen consumption rate.

Peak Torque (PT): The maximum torque that can be obtained from a maximum muscle contraction.

Body Mass Index (BMI): A controversial statistical measurement which compares a person's weight and height.

Maximum Heart Rate (HRmax): The highest number of times a human heart can contract in one minute.

Heart Rate Reserve (HRR): The difference between a person's measured or predicted maximum heart rate and resting heart rate

Rating of Perceived Exertion (RPE): A methods for determining exercise intensity levels. Perceived exertion is how hard one feel his body is working.

Western Ontario and McMaster Universities (WOMAC): A set of standardized questionnaires used to evaluate the condition of osteoarthritis patients.

Kellgren and Lawrence K-L Grade: An x-ray grading system for osteoarthritis that varies from 1 (mild) to severe (grade 4)

American College of Sports Medicine (ACSM): The largest sports medicine and exercise science organization in the world

Enzyme-linked immunosorbent assay (ELISA): A biochemical technique used mainly in immunology to detect the presence of an antibody or an antigen in a sample.

Joint Space Narrowing (JSN): Under pathologic conditions, occurrence of abnormal gap between components of a joint.

Osteoarthritis (OA): A group of diseases and mechanical abnormalities entailing degradation of joints, including articular cartilage and the subchondral bone next to it.

Rheumatoid Arthritis (RA): A chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks the joints producing an inflammatory synovitis that often progresses to destruction of the articular cartilage and ankylosis of the joints.

CHAPTER 2

LITERATURE REVIEW

The purpose of this study was to evaluate the cartilage and bone degradation biomarker changes during a 30-min exercise due to 12-weeks of regular high, medium or non impact exercises. In order to be aware of the responses of articular cartilage to physical exercises, it is essential to review related literature about the cartilage and sport.

This chapter gives basic information about the cartilage and related researches which are fundamental studies constituted background of this study. In this part, literature about (1) Structure of Knee Joint and Articular Cartilage, (2) Evaluation of Knee Joint and Articular Cartilage, (3) Loading on Articular Cartilage and Knee Joint, (4) Sports and Body, (5) Sports and Articular Cartilage, will be mentioned.

2.1 Structure of Knee Joint and Articular Cartilage

Cartilage is one of the rigid connective tissues. It supports parts, provides frameworks and attachments, protects underlying tissues, and forms structural models for many developing bones (Hole, 1989, p. 99). According to Hall, (2005, p. 5) cartilage is deposited by cartilage-forming cells (chondroblasts, chondrocytes) and removed by mono- and multinucleated chondroclasts. Cartilage cells are separated from one another by pericellular and extracellular matrices. Unlike bone cells, chondrocytes lack connecting cell processes. Hall also explained that most chondrocytes continue to divide throughout life, although in some cartilages (mammalian articular cartilages, for example), the number of dividing cells may be less than one percent of the chondrocytes population.

The hydrated ECM of vertebrate cartilage is primarily composed of glycosaminoglycans, notably chondroitin sulphates and proteoglycans. The major collagen is type II, composed of three αII chains, depicted as $\alpha 1(I)_2\alpha II$. Some types of vertebrate cartilages contain additional collagens; for example, type I in articular, fibro and secondary cartilages, and type X in hypertrophic cartilage (Hall, 2005, p. 5).

In their review, Lu & Mow (2008) explained that articular cartilage is a layer of low-friction, load bearing soft tissue that overlies the articulating bony ends in diarthrodial joints. It provides the joint with essential biomechanical functions, such as wear resistance, load bearing, and shock absorption for eight decades or more. However, articular cartilage is an avascular, supporting and articular skeletal tissue, primarily consists of extracellular matrix with a sparse population of cells and it lacks blood vessels, lymphatic vessels and nerves.

Knee joint is the largest joint in the body and it carries the body weight. There are four bones (tibia, fibula, femur and patella) and four ligaments: Medial Collateral Ligament (MCL), Lateral Collateral Ligament (LCL), Anterior Cruciate Ligament (ACL), Posterior Cruciate Ligament (PCL) in a knee joint. Each knee joint has also two crescent-shaped menisci. Also, quadriceps and the hamstrings are two main muscle groups of the knee. By contraction of these muscle groups, the main movements of the knee joint occur between the femur, patella and tibia. Each of these moved bones are covered by articular cartilage which is an extremely hard, smooth substance designed to decrease the frictional forces as movement occurs between the bones (Figure 1).

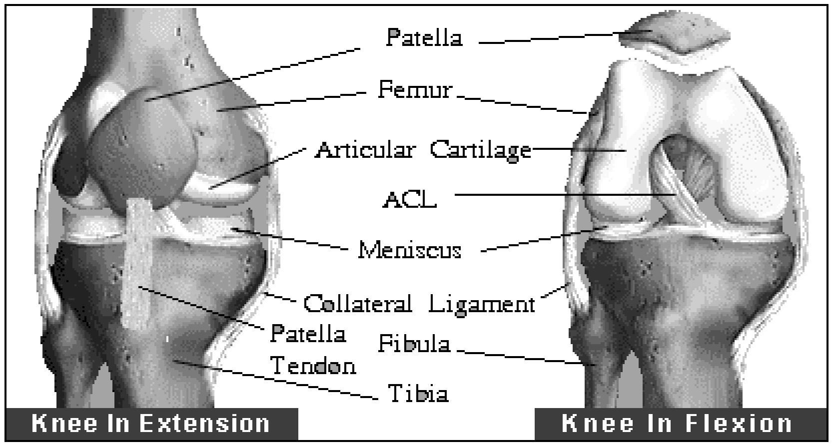

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Figure 1. Structure of Human Knee Cartilage

2.2 Evaluation of Knee Joint and Articular Cartilage

Although the knee joint may look like a simple joint, it is one of the most complexes in all joints. In this complex region, articular cartilage is another complex structure to evaluate. However, a good assessment of the knee joint is important for prevention and rehabilitation of the health. In literature there have been several methods used to assess knee structure and the changes of articular cartilage. New technologies, such as advanced imaging techniques, arthroscopic examinations of joint, biochemical markers of degeneration process, are being used in clinical studies (Kuettner & Goldberg, 1994, p. 481). Also, in literature there are some other methods used to evaluate cartilage of knee like ultrasound or vibration, gait analysis but these latter techniques are not common. Most generally, all these methods have been used to evaluate the structure of cartilage or arthritis which is a disease process that involves uncoupling of the normal balance of degradation and repair in the articular cartilage and subchondral bone (Kuettner & Goldberg, 1994, p. 481).

A very recent but seldom method used in knee cartilage evaluation is vibration method. In a pilot study, Salari and collaborates (2008) used vibration arthrography to evaluate the degree of osteoarthritis in patients. Researchers claimed that vibration arthrography can quantify and visualize the mechanical properties of the knee joint through functional vibration analysis. Result of their study showed that some of the physiological and mechanical properties of the knee cause by abnormalities inside the knee joint are reflected in the vibration signals of the knee.

Another rarely used but old method is ultrasonography. In 1984 Aisen and collaborates assessed real-time ultrasound as a means of evaluating osteoarthritis of the knee. After establishing the validity of the method in an excised bovine knee, 7 asymptomatic individuals, 10 arthritic patients and several patients with other conditions were examined by researchers. At the end of the study Aisen and collaborates claimed that sonography can be used to measure the thickness of the articular cartilage in men, as well as to detect changes on its surface and internal characteristics and early changes of arthritis may be revealed in this manner. Backhaus et al., (1999) compared ultrasonography with some other methods in diagnosis of the arthritis at the finger joints. 32 patients without radiologic signs of destructive arthritis of the evaluated hand and wrist, and 28 patients with radiographs revealing erosions of the evaluated hand and/or wrist were examined in this study. Their data indicated that MRI and ultrasound are valuable diagnostic methods in patients with arthritis who have normal findings on radiologic evaluation. In a recent study Ito and his collaborates (2007), examined the influence of the leg muscle weakness and body mass index on ultrasonography of the knee joint cartilage in middle-aged women. In this study also, researchers mentioned that early screening of the joint cartilage for maintenance and promotion of the health is very important and ultrasound still is a good method for early screening of cartilage deformation.

Kinetic and kinematic characteristics of gait in knee arthritis are another popular research topic. Knee arthritis is a prevalent knee joint degenerative pathology. It is mainly responsible for pain, which occurs when biomechanical constraints are exerted on the knee. Therefore, Viton et al., (1998) analyzed gait patterns of knee arthritis patients. They expected to observe, in unilateral knee arthritis patients, asymmetrical results in the timing of the gait initiation process and in the associated ground reaction forces. Their experimental group was composed of 12 patients with unilateral symptomatic knee arthritis and they excluded patients with pathology that could influence stance and gait. And 12 healthy matched hikers participated in this study as control group. Result of the study demonstrated that the timing of the movement patterns were different in two populations. The initial postural phase was longer when the supporting limb was the affected one than when the sound limb was supporting and than in control subjects. And total movement duration was longer for knee arthritis patients than for control subjects. Researchers concluded that knee arthritis patients develop new posturo motor strategies. Subsequent years, some other researchers investigated the relationship between knee cartilage problems and gait characteristics. However, these researches could not clarify the degenerative condition of articular cartilage.

Bliunas et al., (2002) tested the hypothesis that the peak external knee adduction moment during gait is increased in a group of ambulatory subjects with knee osteoarthritis. Thirty-one participants with radiographic evidence of knee osteoarthritis and medial compartment cartilage damage and thirty-one normal participants (asymptomatic control subjects) with a comparable age, weight and height distribution were tested. In this study, significant differences in the sagittal plane knee motion and peak external moments between the normal and knee osteoarthritis groups were identified using t-tests. Results showed that osteoarthritis group walked with a greater than normal peak external knee adduction moment (P=0.003). The finding of a significantly greater than normal external knee adduction moment in the knee osteoarthritis group lends support to the hypothesis that an increased knee adduction moment during gait is associated with knee osteoarthritis. Same year, Gok, Ergin & Yavuzer (2002) compared the mechanics of gait in 13 patients with early medial arthrosis of the knee and 13 normal controls, by measuring gait events, kinematic and kinetic parameters. Gok and his collaborate also found some differences between the osteoarthritis patients and healthy counterparts during gait analyses. Their findings indicated that computerized gait analysis can be used to reveal various mechanical abnormalities accompanying arthrosis of the knee joint even at early stages. Some of these abnormalities may have etiologic implications, but others may represent secondary changes developed in part as a compensatory mechanism in knee osteoarthritis.

Mundermann, Dyrby, Hurwitz, Sharma & Andriacchi (2004) investigated to potential strategies to reduce medial compartment loading in patients with knee osteoarthritis of varying severity. Their objective was to determine whether reducing walking speed is a strategy used by patients with knee osteoarthritis of varying disease severity to reduce the maximum knee adduction moment. Their findings demonstrated that patients with less-severe OA adapt a walking style that differs from that of patients with more-severe OA and controls. In their study Gok et al., (2002) claimed that gait analysis can be used to reveal knee osteoarthritis even early stages. In addition to this, Mundermann and collaborates observed that gait analysis is a useful method for discriminate the level of severity of knee osteoarthritis. At the another study, Mundermann, Dyrby & Andriacchi (2005) tested the hypothesis that gait changes related to knee osteoarthritis of varied severity are associated with increased loads at the ankle, knee, and hip. Also in this study Mundermann et al. observed different gait characteristics between osteoarthritis patients and control subjects. However, reducing the load at the knee was successful strategy in only patients with less severe knee osteoarthritis. Therefore, Mundermann and her collaborates again demonstrated that gait analyses is an acceptable method for detection and differentiation of knee osteoarthritis.

Radiographic evaluation of knee joint is relatively more common method. Direct measurement of cartilage thickness by radiography is not possible, fundamental principle during radiographic measurement is measuring joint space narrowing. Medial tibia-femoral compartment of the knee and anteroposterior weight bearing view of both knees were the most studied and accepted methods in radiographic assessments of joint space narrowing (Kuettner & Goldberg, 1994, p. 485). During 1990s radiographic evaluation of knee joint status or osteoarthritis of the knee joint is believed to be the most common manifestation of pathology in this joint and different grading systems have been used, for example the Kellgren & Lawrence system and the Ahlbäck classification (Petersson, Boegard, Saxne, Silman & Svensson, 1997). Petersson and coworkers used radiographic measurements and used these two different radiographic grading systems to determine the prevalence of tibiofemoral radiographic knee osteoarthritis (OA) in people aged 35–54 years associated with chronic knee pain. The prevalence of radiographic tibiofemoral OA combined with chronic knee pain in people aged 35–54 years was around 1% as estimated by either the Kellgren & Lawrence or the Ahlbäck classifications systems. This association between grading systems in radiographic measurements in this relatively young age groups demonstrated the accuracy of the methods.

During radiographic evaluation of the knee, the progression of the osteoarthritis can be monitored by measuring the minimum joint space width between the edges of the femoral condyle and the tibial plateau. However, Duryea, Peterfy, Gordon & Genant (2000) claimed that this method needs a trained physician using a graduated magnifying lens and is prone to the subjectivity and variation associated with observer's measurements. Therefore, Duryea and his collaborates developed a software that performs this measurement automatically on digitalized radiographs. The reproducibility of software measurements was representing an improvement of approximately a factor of 2 over manual measurement. The algorithm also showed excellent agreement with the hand-drawn contours and with minimum joint space width determined by the manual method. This software have been used subsequent years by different researchers (Duryea, Zaim & Genand 2003; Lindsey et al., 2004) but positioning of knee is still a reproducibility limitation of the method. In addition to these, Backhaus et al., (1999) reported that cartilage destruction in some arthritis patients is detected by MRI but not by radiological assessment. Also, Kuettner & Goldberg (1995, p. 10) explained that the majority of epidemiologic and clinical studies of the arthritis over 40 years have used plain radiographs to detect different features. The atlas-based Kellgren and Lawrence criteria, which differentiate four grades of disease, have been the "gold standart" until recently. However, Kuettner & Goldberg summarized three major problems of radiographic diagnostic criteria: 1. they lack sensitivity; joint damage needs to be extensive before changes are seen on the plain radiographs. 2. The emphasis is on bone changes; bony abnormalities are easier to see and grade than the changes in the joint space that constitutes the only way cartilage disease can be detected. 3. Radiographic scoring is subjective and has poor reproducibility. Also, Raynauld et al., (2004) evaluated the changes in volume of osteoarthritic knee cartilage over a two-year period with the use of MRI and correlated the MRI changes with radiologic changes. In their study, no statistical correlation between loss of cartilage volume and radiographic changes was seen. Therefore, researchers indicated that radiological changes are not sensible enough to identify patients with rapidly progressing disease.

Magnetic Resonance Imaging (MRI) is a relatively new technology but today it is widely considered as a sensitive and reliable diagnostic method to study the morphological changes of joint cartilage. According to Potter, Linklater, Allen, Hannafin & Haas (1998) MRI has a sensitivity of 87 %, a specificity of 94 %, an accuracy of 92 %, a positive predictive value of 85 % and a negative predictive value of 95 % for the detection of a chondral lesion. Interobserver variability was minimum. Researchers reported that with use of this method, it is possible to asses all articular surfaces of the knee accurately. Also Eckstein et al., (1996) analyzed the accuracy and precision with which the quantitative distribution of articular cartilage can be determined in the knee joint using MRI. They found the reproducibility of intraobserver and interobserver very high in both the specimens and the volunteers. In 1998, Eckstein and collaborates investigated the in vivo reproducibility of volume and thickness measurements from replicated data sets, applying three-dimensional (3D) post-processing methods. Because, previous studies suggested that MR imaging is capable of providing accurate data on knee joint cartilage volume and thickness in vitro, but the reproducibility of these data in living subjects had not been analyzed rigorously. Eckstein and coworkers concluded that MR imaging can be used to determine cartilage volume and thickness in the knee joints of living subjects with high precision, provided that a fat-suppressed gradient-echo sequence with adequate resolution and 3D digital image processing are used. After the evaluation of accuracy of MRI for cartilage thickness measurements, Cohen et al., (1999) assessed the 3D accuracy of MRI for measuring articular surface topographies and cartilage thicknesses of knee joints, by comparison with the calibrated stereo-photogrammetric (SPG) method. In this study, for each bone of the knee, accuracies were most favorable in the patella, followed by the femur and then the tibia. Their results demonstrated that clinical MRI can provide accurate measurements of cartilage topography, thickness, contact areas and surface curvatures of the knee.

Subsequent years, Faber et al., (2001) compared the cartilage thickness, volume, and articular surface areas of the knee joint of young healthy, non-athletic female and male individuals with MRI method. In this study, women displayed smaller cartilage volumes than men. Differences in cartilage volume are primarily due to differences in joint surface areas (epiphyseal bone size), not to differences in cartilage thickness. Their finding demonstrated significant gender differences in cartilage volume and surface area of men and women, which need to be taken into account when retrospectively estimating articular cartilage loss in patients with symptoms of degenerative joint disease.

Magnetic Resonance Imaging was also used to follow progressive cartilage loss in knee at longitudinal researches. In a longitudinal MRI study Biswal et al., (2002) evaluated the risk factors for progressive cartilage loss in the knee in forty-three patients. Result of this study showed that the presence of meniscal and ACL tears was associated with more rapid cartilage loss. Also, researchers reported that MRI can detect interval cartilage loss in patients over a short period.

Hohe, Ateshian, Reiser, Englmeier & Eckstein, (2002) worked on the development of an MR-based technique for quantitative analysis of joint surface size, surface curvature, and joint incongruity and for assessing its reproducibility under in vivo imaging conditions. By this study, Hohe and collaborates 1. implemented a technique for quantitative determination of the size, curvature, and incongruity of articular surfaces from MRI; 2. determined the interscan reproducibility of these parameters in the human knee under in vivo imaging conditions; and 3. assessed differences in these parameters between different compartments of the human knee as well as between different individuals. Researchers claimed that MRI will permit identification of the specific role of surface size, curvature, and incongruity as potential risk factors for osteoarthritis.

Hunter, March & Sambrook (2003) examined the association between knee pain and MRI cartilage volume. In this cross-sectional study, researchers assessed the association between knee symptoms and MRI cartilage volume in an unselected, community based population. The participants were 133 postmenopausal females. Femoral, tibial and patella cartilage volumes were measured using 3D Slicer. In this study qualitative data relating to symptoms, stiffness, pain, physical dysynovial fluid unction and the quality of life using the WOMAC were recorded. Results showed that more knee pain was associated with only severity of patella cartilage reduction. Other MRI cartilage volume features were not strongly associated with WOMAC sub-scores. Following years different researchers analyzed the correlation of knee cartilage volume measured by MRI with several parameters. Nishimura et al., (2005) evaluated the correlation of some physical characteristics and the articular cartilage volumes of the patella and femur in the human knee joints of healthy adults using MRI. They found that cartilage volume was significantly larger in men than in women. However, the volume positively correlated with body weight, height, leg length, and foot size, without distinction of gender or age. According to the correlation results, researchers developed a multiple regression analysis and they concluded that the cartilage volume depends on physical size regardless of gender, and it can be estimated from factors of physical size.

In a review article, Eckstein & Glaser (2004) reviewed works on the assessment of cartilage morphology with quantitative MRI and its relevance to the study of cartilage anatomy, physiology, deformation, disease status, disease progression, and the response to treatment. In this review researchers summarized that quantitative MRI has been shown to provide technically valid and highly precise information on cartilage morphology, particularly at the knee. Therefore Eckstein & Glaser recommended that MRI techniques are powerful and promising tools for cartilage and osteoarthritis research. In another review, Lang, Noorbakhsh & Yoshioka (2005) explained the current state and recent developments of MRI at articular cartilage evaluations. In this review, researchers explained that conventional radiology is widely used in evaluating the long term progression of osteoarthritis by measuring joint space narrowing. However, researchers claimed that conventional radiography is limited by its inability to visualize articular cartilage also during radiographic measurements; highly standardized positioning procedures and even fluoroscopic control of the exact position of the joint are required to obtain reproducible data on joint space narrowing. In their review Lang and his collaborate concluded that MRI offers the distinct advantage of visualizing the articular cartilage directly. MRI can detect signal and morphologic changes in the cartilage and has been used to detect cartilage surface fraying, fissuring, and varying degrees of cartilage thinning.

Another method in the evaluation of the articular cartilage is to use biochemical markers. Biochemical markers in evaluation of cartilage injury and repair are more recent method. Taskiran (2007) explained that articular cartilage is a highly specialized tissue composed of chondrocytes which regulate the metabolism of extracellular matrix molecules responsible for maintaining cartilage function. According to Taskiran, she said:

> Chondrocytes and synoviocytes are metabolically highly active cells and respond to various factors such as hormones, cytokines, growth factors, and mechanical stresses. Under normal physiological conditions, degradation and synthesis of extracellular matrix molecules are maintained in a state of balance. Any disruption of this balance results in degenerative cartilage diseases such as osteoarthritis and rheumatoid arthritis. Currently, diagnoses of both diseases are based on the assessment of a combination of clinical symptoms and radiological findings. However, degenerative changes in the articular cartilage occur long before radiological changes are observed. Therefore, new laboratory tools are required to detect cartilage degradation in the early phase of the disease, to show the progression of cartilage destruction, and to assess response to treatment. In recent years, there has been an increase in the use of some biochemical markers derived from bone and cartilage for the diagnosis and follow-up of cartilage diseases (Taskiran, 2007).

Also, Kuettner & Goldberg (1995. P. 445) stated that abnormal metabolic processes begin in the joint cartilage several years before destruction of the articular surface can be detected radiologically. Also, a noninvasive test for assessing disease progression, examining responses to treatment and evaluating long-term prognosis is essential. Although imaging techniques, such as ultrasonography and MRI, hold promise, the necessary equipments are very costly and not accessible to all (Kuettner & Goldberg, 1995, p. 445). In their book, Kuettner & Goldberg indicated that an exciting new approach consists of measuring cartilage-derived molecules in joint fluid, blood, and urine and then attempting to correlate the levels of these “markers” with metabolic changes taking place in articular cartilage evaluation long before clinical signs of osteoarthritis appear. Williams & Spector (2008) also stated that the favored methods of osteoarthritis assessment are imaging based, with plain radiographs widely used and magnetic resonance imaging (MRI), which remains relatively expensive, used much less. Plain films, however, relate poorly to patient symptoms, and abnormalities occur relatively late in disease.

In a review article Garnero, Rousseau & Delmas (2000) mentioned that the major clinical manifestations of rheumatoid arthritis and osteoarthritis are abnormal and degraded cartilage, synovial, and bone tissues, resulting in severe mobility impairment. Garnero and colleagues explained that specific and sensitive biochemical markers reflecting abnormalities of cartilage, synovium, and bone tissues may be useful for the investigation and monitoring of arthritis.

One of the most-used biochemical markers of the cartilage degradation is Cartilage Oligomeric Matrix Protein (COMP) (Garnero, Rousseau & Delmas, 2000). The COMP is a noncollagenous protein, a glycoprotein, the function of which is to bind to type II collagen fibres and stabilize the collagen fibre network in the articular cartilage (Wislowska & Jablonska, 2005). COMP was first described in 1992 by Hedbom and his collaborates, University of Lund, Sweden. In their study, Hedbom et al., (1992) explained COMP as a specific biochemical marker of bovine fetlock joint articular cartilage. In their study, COMP was found in all cartilages analyzed, but could not be detected in other tissues by enzyme-linked immunosorbent assay of guanidine HCl extracts. Within a given cartilage, COMP shows a preferential localization to the territorial matrix surrounding the chondrocytes. At the end of the same year and from same institution, Forslind K, Eberhardt K, Jonsson A, Saxne T (1992) published an article. In this study, two cartilage specific macromolecules, COMP and proteoglycan were quantified by immunoassay in sera of two groups of patients with rheumatoid arthritis of recent onset to evaluate the prognostic value of such measurements. Patients with rapidly progressive joint destruction had increased COMP concentrations initially, which subsequently decreased. A group with more benign disease, and less extensive joint damage, had normal COMP levels throughout the study period. Serum concentrations of proteoglycan were normal in both groups. Therefore measurement of COMP in serum early in the course of Rheumatoid Arthritis holds promise as a prognostic marker for development of joint destruction in this disease.

Neidhart et al., (1997) determined the tissue distribution of cartilage oligomeric matrix protein in man and evaluated COMP in synovial fluid and serum. COMP was purified from human articular cartilage. Polyclonal antibodies were used to detect COMP in tissue cryosections and protein extracts. COMP was determined quantitatively and qualitatively in synovial fluid and serum by competitive enzyme-linked immunosorbent assay and immunoblotting. Knee joint synovial fluid was taken from nine cadaveric and six living controls, 52 patients with osteoarthritis, 85 patients with rheumatoid arthritis and 60 patients with other forms of inflammatory arthritis. According to their results, the absolute levels of COMP in synovial fluid and serum, and its fragmentation pattern in synovial fluid, seem to be promising as markers of joint tissue metabolism. Synovial fluid and serum level of COMP was also assessed by Kühne et al., (1998). Main objective of their study was to assess whether changes of COMP serum levels can predict the development of osteoarthritis following traumatic knee injury. They acquired sera and synovial fluids at surgery and postoperatively during the first and second year from 30 knee-injured patients. COMP levels and anti-COMP autoantibodies were quantified by ELISA. In their study, results indicated that COMP levels in serum and synovial fluid correlated significantly.

In a cross sectional study Garnero et al.,(2001) evaluated biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis. They correlated these markers with disease activity and joint damage. Researchers analyzed the relations between the urinary levels of type II collagen C-telopeptide (CTX-II) and glucosyl-galactosyl pyridinoline (Glc-Gal-PYD)-two biochemical markers of type II collagen and synovial tissue destruction respectively. In this study, researchers also evaluated serum COMP concentration as a biochemical marker of cartilage degeneration. Garnero and coworkers confirmed that level of serum COMP concentration is higher in patients with knee osteoarthritis than in age matched controls, indicating increased cartilage and synovial tissue turnover.

Larsson et al., (2002) investigated if changes in serum-plasma fibrinogen, hyaluronan and cartilage oligomeric matrix protein levels can be used to differentiate between inflammation and cartilage involvement during arthritis. Fibrinogen was a general inflammation marker, hyaluronan appeared to be a marker for synovitis, and changes in COMP levels appeared to reflect the cartilage destruction process according to the results of this study.

Effect of ethnicity and sex differences on the concentration of potential biochemical markers of osteoarthritis was not described before the Jordan and collaborates' study (2003). In their population-based study of osteoarthritis, they examined associations between serum levels of cartilage oligomeric matrix protein and ethnicity (African American or Caucasian) and sex. They found that in adjusted models, COMP was higher in African American women than in Caucasian women ($P = 0.003$) and higher in Caucasian men than Caucasian women ($P = 0.0001$). There were no statistically significant differences in serum COMP levels between African American men and women. These results show that serum COMP levels vary by ethnicity and sex and differences should be considered in the derivation of standards using this, and possibly other, potential biomarkers of osteoarthritis. Also the heritable determinants of cartilage oligomeric matrix protein were evaluated in literature (Williams et al., 2006). In their research design, a classic twin study was conducted. COMP levels in serum were obtained from healthy female twin volunteers to determine whether genetic factors influence it. The heritability of COMP was determined by comparing correlation among 160 monozygotic and 349 dizygotic twin pairs in this study. Serum levels of COMP showed a correlation of 0.72 among monozygotic twin pairs and 0.47 in dizygotic pairs. Their findings showed that heritable factors influence serum levels of the cartilage matrix biomarker COMP.

Some researchers tried to decrease high serum COMP concentration, which increased during arthritis, by different treatment applications. Crnkic et al., (2003) evaluated changes in serum COMP concentration during a 6-month period from initiation of treatment of rheumatoid arthritis patients with two different compound, infliximab or etanercept. According to their results, serum COMP concentration decreased at third month in both groups of treated patients and remained low until sixth months. In these patient groups, the pattern of changes of serum COMP supports the interpretation that infliximab and etanercept have a joint protective effect. By this study, serum COMP was shown to have potential as a useful marker for evaluating tissue effects of novel treatment modalities in rheumatoid arthritis. Wislowska & Jablonska (2005) compared the serum COMP concentration levels of osteoarthritis and rheumatoid arthritis patients and no statistical differences were found. This study demonstrated that serum COMP level is a useful marker of both osteoarthritis and rheumatoid arthritis.

Vilim et al., (2002) correlated serum level of COMP with radiographic progression of knee osteoarthritis. Serum COMP levels were measured at baseline and at the end of the study, and levels were correlated with changes in joint space width, Kellgren-Lawrence grade, and WOMAC indices, over 3 years. Correlation results indicated that serum COMP has the potential to be a prognostic marker of disease progression. In another longitudinal study, started at the same period with Vilim and coworkers, nonlinear or phased progression of knee osteoarthritis based on measurements of serum cartilage oligomeric matrix protein levels was monitored for five years (Sharif, Kirwan, Elson, Granell, & Clarke, 2004). Serum COMP levels were measured at study entry and every 6 months thereafter in 115 patients with knee pain and osteoarthritis of mainly the tibiofemoral joint. Cartilage loss was determined from knee radiographs taken at entry and at 24, 36, and 60 months. Most important finding of logistic regression analysis in this study was on average, a 1-unit increase in serum COMP levels increased the probability of radiographic progression by 15%. Researchers suggested that serum COMP is related to progressive joint damage in knee osteoarthritis and sequential measurements of serum COMP levels may identify patients whose osteoarthritis is likely to progress over the next year or two.

While some researchers were investigating the effectiveness of COMP as a marker of progressive joint damage, some other research groups started to evaluate the changes of COMP concentration by the effect of mechanic loads. Physical forces are known to influence the synthesis, assembly and degradation of the cartilage extracellular matrix (Giannoni, Siegrist, Hunziker & Wong, 2003). For example marathon runners have an increased risk of developing joint disease, and erosive joint lesions can frequently be observed. Therefore, increased serum level of cartilage oligomeric matrix protein in marathon runners was investigated by Neidhart et al., (2000). They compared the serum levels of COMP between marathon runners, non-running healthy participants and patients with various joint diseases, and they examined whether it can be used as a marker for joint metabolism in sport medicine. In this study Neidhart and colleagues collected serum samples from eight endurance-trained runners shortly before the start of a marathon run, after 31 km, 42 km, 2 h after the end, on the first and on the second morning after the run. For comparison, serum was obtained from 35 healthy controls and 80 patients with knee joint injury, rheumatoid arthritis or osteoarthritis. Their results revealed that, the runner's baseline serum level of COMP was significantly increased when compared with healthy controls. The elevated levels of COMP were similar to those found in joint injury or osteoarthritis. During the run, the serum level of COMP rose significantly and gradually returned to baseline within 24 h. Neidhart concluded that elevated baseline level of COMP might reflect increased joint matrix turnover and/or damage due to prior extreme physical training. During the run, COMP was increasing possibly due to the severe physical strain on joint structures, associated with the early inflammation. Therefore researchers suggested that COMP is a marker for distinct aspects of joint metabolism and/or damage in both disease and sport.

In 2005 Kersting, Stubendorff, Schmidt & Brüggemann, investigated the relationship between running induced joint loading at the knee, changes in cartilage volume and serum COMP concentration. During this study, blood samples and MRI scans were taken before and following a 1h training run in order to determine knee cartilage volume and serum COMP concentration. Individual knee joint loading parameters were calculated from positional data and ground reaction forces, also electromyography was employed to quantify activity of main muscle groups crossing the knee joint. Analysis showed that changes in cartilage volume and COMP showed significant correlations. Also, multiple regression revealed that resting COMP, COMP change after exercise and the time of co-activation of flexor and extensor muscles explain the variance of cartilage volume changes. By means of results Kersting and collaborates concluded that muscular co-activation was the main mechanical parameter related to cartilage changes. Same year, Mündermann, Dyrby, Andriacchi & King (2005) tested the hypothesis that physiological cyclic loading during a 30-min walking exercise causes an increase in serum COMP concentration in a healthy population. Blood samples were drawn from 10 physically active adults immediately before and after, and 0.5h, 1.5h, 3.5h and 5.5h after a 30-min walking exercise on a level outdoor walking track at self-selected normal speed. A significant increase (9.7%; P=0.003) occurred immediately after the walking exercise. Also second increase in serum COMP concentration (7.0%; P=0.024) occurred 5.5h after the walking exercise. Results of this study showed us that; even a moderate walking activity can significantly influence serum COMP concentration. The immediate response points to a diffusion time of COMP fragments from cartilage to the blood of 30 min or less.

By an experimental study Andersson et al., (2006) proved that COMP increase temporarily after physical exercise in patients with knee osteoarthritis. Researchers monitored serum levels of COMP during a randomized controlled trial of physical exercise vs. standardized rest in individuals with symptomatic and radiographic knee osteoarthritis. In this study blood samples were collected from 58 individuals at predefined time points before and after exercise or rest, one training group and one control group. The physical exercise consisted of a one-hour supervised session twice a week and daily home exercises. In a second supplementary study 7 individuals were subjected to the same exercise program and sampling of blood was performed at fixed intervals before, immediately after, 30 and 60 minutes after the exercise session and then with 60 minutes interval for another five hours after the exercise to monitor the short-term changes of serum COMP. Results showed that after 60 minutes exercise serum COMP levels increased ($p < 0.001$) and after 60 minutes of rest the serum levels decreased ($p = 0.003$). Median serum COMP values in samples obtained prior to exercise or rest at baseline and after 24 weeks did not change between start and end of the study. In the second study serum COMP increased immediately after exercise ($p = 0.018$) and had decreased to baseline levels after 30 minutes. Serum COMP levels increased during exercise in individuals with knee osteoarthritis, whereas levels decreased during rest. The increased serum COMP levels were normalized 30 minutes after exercise session, therefore it is suggested that samples of blood for analysis of serum COMP should be drawn after at least 30 minutes rest in a seated position. No increase was seen after a six-week exercise program indicating that any effect of individualized supervised exercise on cartilage turnover is transient. These studies demonstrated that COMP is a sensitive biomarker of cartilage degradation and increase temporarily after physical exercise.

There are some other biochemical markers of the cartilage degradation. C-terminal telopeptides of type II collagen (CTX-II) as marker of cartilage destruction and C-terminal telopeptides of type I collagen (CTX-I) as marker of bone destruction may be other most common markers in osteoarthritis research. CTX-II was first used in 2001 by Christgau and his collaborates. In this study, researchers reported the development of an assay for measurement of the urinary concentration of collagen type II C-telopeptide fragments. They developed this assay for providing a specific marker of joint metabolism. And Christgau and colleagues claimed that this assay showed high technical precision and an ability to differentiate populations with an elevated joint metabolism from normal controls. This suggests that the assay may have clinical value in assisting in the diagnosis of joint diseases and in monitoring progression and therapy in rheumatoid arthritis and osteoarthritis. Today, manufacturer of CTX-II Elisa kit explains the intended use of marker for in vitro diagnostic use as an indication of degradation of cartilage and may be used as an aid for 1. quantitative assessment of disease activity (structural damage of articular cartilage) in patients with rheumatoid arthritis and osteoarthritis, 2. prognosis of disease activity in patients with rheumatoid arthritis and osteoarthritis, and 3. early assessment of long-term effect of therapy in patients with rheumatoid arthritis.

Same year, Garnero et al, (2001) made a research about this newly developed biochemical markers of type II collagen. In a part of this study, the relations between the urinary levels of CTX-II, disease activity and the severity of joint destruction in patients with knee osteoarthritis was analyzed. CTX-II was also correlated with pain and physical function (WOMAC index). Results showed that CTX-II was an important predictor of the WOMAC index and joint damage. Therefore, researchers claimed that CTX-II may be useful marker of disease severity in patients with knee osteoarthritis. In 2002, Garnero et al., mentioned the limitations of radiological evaluation of rheumatoid arthritis and they sought to determine whether urinary C-terminal crosslinking telopeptide of type I (CTX-I) and type II (CTX-II) collagen (markers of bone and cartilage destruction, respectively) are associated with long-term radiologic progression in patients with early rheumatoid arthritis. They investigated the relationship between baseline levels of urinary CTX-I and CTX-II and the mean annual progression of joint destruction over a median of 4 years. In this study high baseline level of urinary CTX-I and CTX-II independently predict an increased risk of radiologic progression over 4 years in patients with early rheumatoid arthritis. Garnero and his collaborates concluded that urinary CTX-I and CTX-II may be useful for identifying individual rheumatoid arthritis patients at high risk of progression very early in the disease, before erosions can be detected radiographically. Then Garnero et al., (2003) published an extended report about the changes of urinary CTX-II level in patients with rapidly destructive hip osteoarthritis. They compared type II collagen degradation using CTX-II in patients with rapidly destructive and those with slowly progressive hip osteoarthritis. In this study, patients with hip osteoarthritis had higher mean urinary CTX-II levels than healthy age matched controls. Also researchers indicated that increased urinary CTX-II correlated significantly with decreased minimum joint space width assessed by radiograph of the hip. Researchers also evaluated urinary free deoxypyridinoline, a marker of bone resorption in this study but there was no significant difference between patients and controls in measured parameters. Increased urinary CTX-II levels are associated with rapidly destructive disease in this study. Therefore, results suggest that this marker might be useful in identifying patients with hip osteoarthritis at high risk for rapid progression of joint damage.

Forsblad d'Elia et al., (2004) evaluated the effects of hormone replacement therapy on markers of bone and cartilage metabolism. Also they assessed whether changes in these markers corresponded to alterations in bone mineral density and radiographic joint destructions in postmenopausal women with rheumatoid arthritis. CTX-I was one of the bone turnover markers in this study and urinary CTX-II and serum COMP were use as cartilage turnover markers. Treatment with hormone replacement therapy resulted in decrease in CTX-I ($P < 0.001$), COMP ($P < 0.01$), and CTX-II ($P < 0.05$) at 2 years. Based on these results, it was indicated that biochemical markers of bone and cartilage turnover may provide a useful tool for assessing novel treatment modalities in arthritis, concerning both joint protection and prevention of osteoporosis. Subsequent year, CTX-II was correlated with new cartilage degradation biochemical marker as a high standard. Charni, Juillet, & Garnero (2005) worked on developing a new biochemical marker reflecting the degradation of the helical region of type II collagen and evaluated its clinical performance in patients with osteoarthritis and rheumatoid arthritis. In this study, results demonstrated that patients with increased levels of both urinary HELIX-II and CTX-II had the highest risk of progression.

Ding et al., (2005) evaluated the associations between knee cartilage defects and knee radiographic osteoarthritis, cartilage volume, bone size and type II collagen breakdown in adults. In multivariate analysis, the severity and prevalence of knee cartilage defects were significantly and independently associated with tibiofemoral osteophytes and tibial bone area. Knee cartilage defects were inconsistently associated with joint space narrowing after adjustment for osteophytes but consistently associated with knee cartilage volume. Lastly, knee cartilage defect severity was significantly associated with urinary CTX-II. Ding and coworkers summarized that knee cartilage defects may result in increased cartilage breakdown leading to decreased cartilage volume and joint space narrowing suggesting an important role for knee cartilage defects in early knee osteoarthritis. Also, Raissouni, Gossec, Ayral, & Dougados, (2005) stated that treatment for rheumatoid arthritis should be initiated early, if possible within the first six months after symptom onset, and should be selected according to the potential for disease progression. Early initiation of combination drug therapy may improve quality of life and long-term outcomes. Therefore, investigators reviewed the literature comprehensively to identify factors predicting chronic arthritis and joint destruction. In this review Raissouni and collaborates concluded that high levels of CTX-I and CTX-II strongly predict the development of joint erosion before the occurrence of radiographical joint damage. However, a threat was indicated by Garnero, Sornay-Rendu, Arlot, Christiansen, & Delmas, (2004) when analyzing levels of CTX-II in studies of knee, hip, and hand osteoarthritis. In a group of postmenopausal women, disc space narrowing and osteophytes were scored. Femorotibial knee osteoarthritis was assessed by radiographs. For all women, hand osteoarthritis was assessed by clinical examination. Also, level of urinary CTX-II was measured. Results revealed that patients with lumbar spine disc space narrowing, knee osteoarthritis and clinical hand osteoarthritis had CTX-II levels 80% higher than those of patients with no lumbar spine disc space narrowing, no radiologic knee osteoarthritis, and no clinical hand osteoarthritis. Postmenopausal women with lumbar spine disc degeneration were characterized by increased CII degradation. By this study, researchers exhibited that Lumbar spine disc degeneration in elderly patients should be assessed when analyzing levels of CTX-II in studies of knee, hip, and hand osteoarthritis.

In a very recent study, correlation of CTX-I and CTX-II with radiological changes at baseline and after 2 years follow-up in patients with ankylosing spondylitis was evaluated (Vosse et al., 2008). Ankylosing spondylitis is a chronic inflammatory disease mainly affecting the axial skeleton and is characterized by ossification of the spinal joints and ligaments. In this study, eighty-three patients with ankylosing spondylitis were assessed for urinary CTX-I and CTX-II. Results of both biochemical markers were compared with baseline scores for radiological damage, and with scores for radiological progression after 2 years follow-up. Analysis showed that baseline radiological damage correlated with CTX-II, but not with CTX-I. In multivariate analyses, CTX-II significantly and independently contributed to explaining variation in radiological damage and progression. It was concluded that cartilage degradation, and therefore, CTX-II increase plays a role in explaining radiological-damage and -progression in the spine.

In spite of developing new biochemical markers, COMP is still unique in all biochemical markers of cartilage degradation or osteoarthritis. In an editorial article in Arthritis Research & Therapy journal, Williams and Spector (2008) explained that biomarkers aid the study of osteoarthritis in a number of different ways and COMP is foremost among hitherto investigated biomarkers and is most consistently shown to predict knee osteoarthritis progression. Similar finding were stated by Hunter and collaborates (2007). In their longitudinal observation study Hunter et al., reported that among subjects with symptomatic knee osteoarthritis, a single measurement of increased COMP predicted subsequent cartilage loss on MRI. In addition to this, with the exception of COMP, none of the other biomarkers was a statistically significant predictor of cartilage loss.

2.3 Loading on Articular Cartilage and Knee Joint

In daily life, cyclic loading is the most common mode of loading in human lower limb joints. These joints are subjected to 1 to 4 million load cycles per year on average during walking activity (Seedhom and Wallbridge, 1985). In addition to walking activity, in daily life some other activities are loaded on knee joint. Mundermann, Dyrby, D'Lima, Colwell, & Andriacchi, (2008) examined the relationship between activity, peak load, medial to lateral load distribution, and flexion angle at peak load for activities of daily living. They measured knee joint force simultaneously with motion capture during walking, chair sit to stand and stand to sit, stair ascending and descending, squatting from a standing position, and golf swings. For all activities, total compressive load on knee joint exceeded 2 times body weight, and for most activities 2.5 times body weight. This amount of physiological cyclic load causes a deformational behavior of articular cartilage. In a normal joint, there is a balance between the production of new collagen and proteoglycans, and the breakdown of aging molecules. However, mechanical and biochemical responses of articular cartilage for disuse and overuse have been interesting subjects for researchers.

The potential for loss of bone mineral mass due to space flight was recognized by space scientists even before man's first venture into micro-gravity (LeBlanc, Spector, Evans, & Sibonga, 2007). However, knowledge about the effect of microgravity or unloading on articular cartilage was limited up to recent years. Vanwanseele, Lucchinetti, & Stussi (2002) reviewed current data and concepts concerning the effect of immobilization on articular cartilage in animal models. They also evaluated the methods to measure articular cartilage changes in human. In this study, effects of immobilization on morphological, biochemical, and biomechanical characteristics of articular cartilage were reviewed. Results revealed that articular cartilage changes in immobilized animals include altered proteoglycan synthesis, as well as thinning and softening of the tissue. The overall thickness of articular cartilage in the knee decreases up to 9% after 11 weeks of immobilization. This study summarized that alterations in the morphologic, biochemical, and mechanical properties of cartilage occur after unloading and immobilization in animals. However, the findings have been inconsistent and it is unclear whether such changes also take place in human. Therefore, Vanwanseele, Eckstein, Knecht, Stüssi, & Spaepen, (2002) tested the hypothesis that progressive thinning of knee joint cartilage is observed after spinal cord injury. They assessed the knee cartilage of patients with complete, traumatic spinal cord injury at 6 (n = 9), 12 (n = 11), and 24 months (n = 6) after injury. Morphologic parameters of the knee cartilage were compared with those in young, healthy volunteers. Results showed that after 6 months of injury, the mean articular cartilage thickness was significantly less in the patella and medial tibia (decrease of 10% and 16%, respectively), but not in the lateral tibia (decrease of 10%), compared with the MRI findings in healthy volunteers. After 12 and 24 months of injury, the differences amounted to a reduction of 21% and 23%, in the patella, 24% and 25%, in the medial tibia, and 16% and 19%, in the lateral tibia, respectively. The changes were significant in all 3 surfaces of the spinal cord-injured joint cartilage. This data showed that progressive thinning of human cartilage occurs in the absence of normal joint loading and movement.

After this cross-sectional study, Vanwanseele, Eckstein, Knecht, Spaepen, & Stussi, (2003) performed a longitudinal analysis of cartilage atrophy in all knee compartments, including the femoral condyles, in spinal cord injury patients over 12 months. They examined the right knees of 9 patients with complete, traumatic spinal cord injury shortly after the injury and at 6 and 12 months post-injury. Results demonstrated that the mean thickness of knee joint cartilage decreased significantly during the first 6 months after injury (range 5-7%). The mean change at 12 months was 9% in the patella, 11% in the medial tibia, 11% in the medial femoral condyle, 13% in the lateral tibia, and 10% in the lateral femoral condyle. This study indicated that human cartilage atrophies in the absence of normal joint loading and movement after spinal cord injury, with a rate of change that is higher than that observed in osteoarthritis.

Immobility studies indicated that regular use of articular cartilage is essential for its health. We know that daily activities cause some impact on weight bearing sides of articular cartilage. Quantification and characterization of the deformation behavior of articular cartilage when subjected to physiological cyclic loading have a fundamental importance. In order to quantify the responses of cartilage, some researchers evaluated the ground reaction forces, impact-absorption properties, deformational and adaptational behavior of articular cartilage.

In a biomechanical study, Hoshino, & Wallace, (1987) investigated load-absorbing mechanism of 20 cadaveric knees. The impact load was applied using a weight falling onto the transected proximal femur and the force transmitted through the knee was measured at the transected distal tibia using a load transducer. In this study, results showed that the joint has an impact-absorbing property in each segment.

Articular cartilage is the thin layer of deformable, load-bearing material which lines the bony ends of all diarthrodial joints. When an external load is applied to a joint, articular cartilage deforms, resulting in increased joint contact areas and decreased contact stresses (Setton, Elliott, & Mow, 1999). Setton et al. explained that, in a healthy joint, articular cartilage may provide load-bearing, energy dissipation and joint lubrication with little or no signs of wear. With injury or degeneration related to osteoarthritis, cartilage changes which are associated with significant loss of mechanical function will occur, with the potential to cause further progressive degeneration of cartilage.

Abnormal transmission of loads may result in osteoarthritis. Fukuda et al., (2000) evaluated the role of the cancellous bone in these processes and load transmission in the cancellous bone of the tibia under static and impact load. In this study, the compressive stresses in the subchondral bone, epiphysis and diaphysis of the tibia of porcine knees were measured under static and impact load using mini-pressure transducers. Tests were repeated after meniscectomy and after removing the articular cartilage. Results showed that in the intact knee in all alignments, the highest stress on the medial side was found in the epiphysis, and in the subchondral bone on the lateral side. After meniscectomy, a significant increase was observed in the stress on both sides of the subchondral bone. After the removal of the articular cartilage, the stress in the subchondral bone increased again, but slightly.

The growth, maintenance and ossification of cartilage are fundamental for skeletal development and are regulated throughout life by the mechanical cues that are imposed by physical activities. In their computer modeling study, Carter & Wong (2003) indicated that local intermittent hydrostatic pressure promotes cartilage maintenance. Cyclic tensile strains (or shear), however, promote cartilage growth and ossification. They explained that in the middle and deep layers of articular cartilage, the cartilage phenotype is maintained by cyclic fluid pressure. In superficial articular layers the chondrocytes are exposed to tangential tensile strain in addition to the high fluid pressure. Researchers concluded that computer model predictions of cartilage mechanobiology are consistent with the results of in vitro cell, tissue and molecular biology experiments. According to Wong & Carter (2003) the histomorphogenesis of articular cartilage is regulated during skeletal development by the intermittent forces and motions imposed at diarthrodial joints. In a mature joint, cyclic loads produce cyclic hydrostatic fluid pressure through the entire cartilage thickness that is comparable in magnitude to the applied joint pressure. Prolonged physical activity can cause the total cartilage thickness to decrease about 5%. The topological variation in the histomorphologic appearance of articular cartilage is influenced by the local mechanical loading of chondrocytes in the different zones.

Henderson et al., (2007) stated that experimental and theoretical researches show that mechanical stimuli may play a role in morphogenesis. Therefore, Henderson and collaborates investigated whether theoretically predicted patterns of stress and strain generated during the growth of a skeletal condensation are similar to in vivo expression patterns of chondrogenic and osteogenic genes. Their analysis showed that predicted patterns of compressive hydrostatic pressure correspond to the expression patterns of chondrogenic genes, and predicted patterns of tensile strain correspond to the expression patterns of osteogenic genes. Furthermore, the results of the analysis suggested that stresses and strains could promote the formation and refinement of stiff tissue surrounding the condensation, a prediction that is in agreement with an observed increase in collagen bundling surrounding the cartilage condensation, as indicated by picro-sirius red staining. These results are consistent with mechanical stimuli playing an inductive or maintenance role in the developing cartilage and associated perichondrium and bone collar. This theoretical analysis provides insight into the potential importance of mechanical stimuli during the growth of skeletogenic condensations.

2.4 Sports and Body

Shifts from hunting and gathering to agriculture, and then to industry, have changed physical activity patterns markedly since the Stone Age, which has improved mankind's health vitality and longevity. The importance of physical activity and physical fitness to health and longevity has long been featured through the writings of the Ancients (Paffenbarger, Blair, & Lee 2001). Also, MacAuley (1994) reported that the importance of physical development in early eastern civilizations had been recorded in many tomb drawings. Even in primitive society, physical culture was important, often ritualized into dance and similar activity (MacAuley, 1994). More than 2000 years ago, Hippocrates advised us that exercise, through not too much of it, was good for health (Hippocrates, as cited in Paffenbarger, 2001).

From early ages to today's knowledge about the physical activity for physical fitness has developed apace with new methods of researches. According to Housh et al, (2003) in modern ages, discussion about physical fitness frequently evolved into arguments about physical fitness for what? Today we have enough scientific evidence to answer this question with a simple statement: Optimal level of physical activity and fitness are conducive to lifelong good health. In this regard, U.S. Department of Health and Human Services published a report on Physical Activity and Health (1996). Major conclusions of this report were:

1. People of all ages, both male and female, benefit from regular physical activity.

2. Significant health benefits can be obtained by including a moderate amount of physical activity (e.g., 30 minutes of brisk walking or raking leaves, 15 minutes of running, or 45 minutes of playing volleyball) on most, if not all, days of the week. Through a modest increase in daily activity, most Americans can improve their health and quality of life.

3. Additional health benefits can be gained through greater amounts of physical activity. People who can maintain a regular regimen of activity that is of longer duration or of more vigorous intensity are likely to derive greater benefit.

4. Physical activity reduces the risk of premature mortality in general, and of coronary heart disease, hypertension, colon cancer, and diabetes mellitus in

particular. Physical activity also improves mental health and is important for the health of muscles, bones, and joints.

5. More than 60 percent of American adults are not regularly physically active. In fact, 25 percent of all adults are not active at all.

6. Nearly half of American youths 12–21 years of age are not vigorously active on a regular basis. Moreover, physical activity declines dramatically during adolescence.

7. Daily enrollment in physical education classes has declined among high school students from 42 percent in 1991 to 25 percent in 1995.

8. Research on understanding and promoting physical activity is at an early stage, but some interventions to promote physical activity through schools, worksites, and health care settings have been evaluated and found to be successful.

Numerous scientific studies confirmed that many health and fitness benefits derived from regular physical exercises (de Assis et al., 2008; Bucksch, 2005; Dolezal & Potteiger 1998; Karlsson, Nordqvist & Karlsson, 2008; Inoue et al., 2008; Salci et al., 2001; Wong et al., 2008). Also, American College of Sports Medicine (2001) summarized the benefits of regular physical activity and exercise as improvements in cardiovascular and respiratory functions, reduction in coronary artery disease risk factors, decrease in mortality and morbidity. Also, decreased anxiety and depression, enhanced feelings of well-being and, enhanced performance of work, recreational, and sport activities were reported as other postulated benefits of regular exercise in this guideline.

In their study, Wong and her collaborates (2008) investigated the effects of a 12-week twice weekly additional exercise training, in additional to typical physical education sessions, on aerobic fitness, body composition and serum C-reactive protein (CRP) and lipids were analyzed in 13 to 14 year old obese boys contrasted with a control group. At the end of the study researchers observed that exercise training significantly improved lean muscle mass, body mass index, fitness, resting HR, systolic blood pressure and triglycerides in experimental group. This study supports the value of exercise training program, to produce physiological benefits in the management of obesity in adolescents.

Relationship between physical activity and bone mineral density has been another popular subject in recent years. Salci et al. (2001) investigated the relationship between bone mineral density and physical activity level of physically active and sedentary women between 19-40 ages. Result of this study demonstrates that practicing regular physical activity in early ages has an improving effect on bone mineral density values. Also, sustainability of exercise-induced increases of bone mineral density was questioned in a review by Karlsson et al. (2008). In this study, researchers evaluated if exercise-induced skeletal benefits achieved during growth remain in a long-term perspective. Publications within the field were searched through Medline using the search words: exercise, physical activity, bone mass, bone mineral content (BMC), bone mineral density (BMD) and skeletal structure. Results of this study demonstrated that benefits of exercise on BMD during growth seem to be eroded at retirement, but benefits in skeletal structure may possibly be retained in a longer perspective. Karlsson and his collaborates concluded that exercise during growth may be followed by long-term beneficial skeletal effects, which could possibly reduce the incidence of fractures.

In a follow up study, Bucksch (2005) examined the effect of moderately intense physical activity on all cause mortality in a sample composed of men and women. Findings of the this study confirm that physical activity of moderate intensity not less than the recommendation of CDC (Centers for Disease Control and Prevention)/ACSM (American College of Sports Medicine) is sufficient to prevent premature death, but this effect was only seen in the female sample. In men, only physical activity of vigorous intensity predicted a clear risk reduction.

Physical activity and cancer is another popular research topic in literature. In a very recent study Inoue et al. (2008) prospectively examined the association between daily total physical activity and subsequent cancer risk in the Japan Public Health Center based Prospective Study. The decreased risk was more clearly observed in women than when compared with men, especially among the elderly and those who regularly engaged in leisure-time sports or physical exercise. By site, decreased risks were observed for cancers of the colon, liver, and pancreas in men and for cancer of the stomach in women. Researcher concluded that increased daily physical activity may be beneficial in preventing cancer in a relatively lean population.

Lee, Rexrode, Cook, Manson, & Buring, (2001) stated that physically active women have lower coronary heart disease rates than inactive women. However, whether the association differs by intensity of activity or in women at high risk for coronary heart disease is unclear. Therefore, they examined the relation between physical activity and coronary heart disease among women, including those at high risk for coronary heart disease. 39372 healthy female health professionals were participated in this Cohort study from 1992 to 1999. A total of 244 cases of coronary heart disease occurred during this period. Vigorous activities were associated with lower risk of coronary heart disease. Walking also predicted lower risk among women without vigorous activities. Measured data of this investigation indicated that even light-to-moderate activity is associated with lower coronary heart disease rates in women.

2.5 Sport and Articular Cartilage

The father of medicine, Hippocrates, indicated following: "All parts of the body which have a function, if used in moderation and exercised in labors in which each is accustomed, become thereby healthy, well-developed and age more slowly, but if unused and left idle they become liable to disease, defective in growth, and age quickly" (Hippocrates, as cited in Leon, Myers, & Connett, 1997). This view was proved for most of the tissues by modern researchers. During last decades researchers evaluated the changes of bone and muscle by the effect of exercises (Taaffe, Robinson, Snow, & Marcus, 1997; Salci et al., 2001). However, permanent effect of exercise on articular cartilage has not been established clearly for articular cartilage.

Preliminary studies about the effect of physical exercise on articular cartilage generally performed on animal models. Kiviranta, Tammi, Jurvelin, Saamanen, & Helminen, (1988) evaluated the effect of moderate running exercise on glycosaminoglycans and thickness of articular cartilage in the knee joint of young beagle dogs. The local influences of physical exercise on thickness and glycosaminoglycan content of canine articular cartilage were measured by microspectrophotometry. Beagle dogs were divided into runner (n = 6) and control (n = 8) groups and the training program started at the age of 15 weeks. At the age of 40 weeks, the samples for histology were taken from 11 different anatomical locations of the right knee joint. In this study, the thickness of the uncalcified cartilage increased 19-23% on the lateral condyle and patellar surface of the femur, whereas the enhancement was smaller in other parts of the trained cartilage. Total glycosaminoglycans were augmented by 28% in the summits on the femoral condyles, more on the medial than lateral side. According to these results, researchers judged that enhanced glycosaminoglycan content and thickness shows that moderate running exercise locally alters the biological properties of young articular cartilage at regions bearing the highest loading surplus. In another animal study, Lammi et al., (1993) evaluated the adaptation of canine femoral head articular cartilage to long distance running exercise in young beagles. The effects of long term (one year), long distance (up to 40 km/day) running on the metabolism of articular cartilage the biosynthesis of proteoglycans was examined by in vitro labeling of anterior (weight bearing) and posterior (less weight bearing) areas of the femoral head from young beagles. Like previous study, the articular cartilage of the femoral head showed a great capacity to adapt to the increased mechanical loading in present study.

In another study on canine, Qi & Changlin (2007) examined the association between levels of COMP, and some other cartilage biomarkers with MRI of cartilage degeneration in knee joint. Also, they evaluated the effects of movement training with different intensity on cartilage of knee joint. 20 adult canines were divided into light training, intensive training and control groups. The training lasted for 10 weeks. MRI examinations were performed regularly (2nd, 4th, 6th, 8th, 10th week) to investigate the changes of articular cartilage in the canine knee, while concentrations of biomarkers were measured. They found significant differences between training groups and control group in MRI results. However, there was no significant difference between training groups. Elevations of levels of COMP, MMP-1, MMP-3, TIMP-1, MMP-3/TIMP-1 were seen in serum and synovial fluid after training, and their levels had obvious association with knee MRI grades of cartilage lesion. Furthermore, there were statistically significant associations between biomarkers' levels in serum and in synovial fluid. Long-time and high-intensity movement training induces cartilage degeneration in knee joint. Within the intensity extent applied in this study, knee cartilage degeneration caused by light or intensive training has no difference in MR imaging, but has a comparatively obvious difference in biomarkers' level. To detect articular cartilage degeneration in early stage and monitor pathological process, the associated application of several biomarkers has a very good practical value, and can be used as a helpful supplement to MRI. In another study, Qi, Changlin, & Zefeng, (2007) evaluated the cartilage injury of knee joint in a rabbit model under high-intensity jumping training. They used matrix metalloproteinase-1 (MMP-1), matrix metalloproteinase-3 (MMP-3), and tissue inhibitor of matrix metalloproteinase-1 (TIMP-1) in synovial fluid to predict early sports injury of articular cartilage effectively. Rabbits were divided into two groups of untreated control and jumping training groups. Researchers measured the concentrations of biological markers at 4th and 8th weeks. Results demonstrated that sulfated GAG content, thickness of subchondral bone, and Mankin grades in training group were significantly higher than control at the end of the 4 weeks. After 8 weeks, the training group had a further increase in the articular cartilage injury and the level of these biomarkers was significantly associated with the severity of the articular cartilage pathology. According to this result, researchers concluded that repetitive and high-intensity jumping movement may induce sports injury in the knee joint cartilage.

Brommer et al., (2005) evaluated the functional adaptation of articular cartilage under the influence of loading in foals. Osteochondral plugs were drilled out from impact-loading and constant loading sites of stillborn, 5 months, 18 months and mature horses. Researchers observed that fetal cartilage was significantly thicker compared to the other ages with no further age-dependent differences in cartilage thickness from age 5 months onwards. According to these findings, after 18 months age, no major adaptations seem to occur. Therefore researchers concluded that functional adaptation of biomechanical properties takes place early in life for horses.

Early studies about the effect of sport or exercise on human articular cartilage were commonly cross-sectional studies. Generally, current conditions of elite athletes or industrial workers were compared with control counterparts in these studies. One of pioneer study, Mühlbauer, Lukasz, Faber, Stammberger & Eckstein, (2000) compared knee joint cartilage thickness of triathletes with those of physically inactive volunteers. The right knee joints of nine male triathletes and nine inactive male volunteers were imaged with a fat-suppressed gradient echo sequence. It is reported that in the patella, the femoral trochlea, and the lateral femoral condyle, the mean and maximal cartilage thickness values were slightly higher in triathletes, but they were somehow lower in the medial femoral condyle, and in the medial and lateral tibial plateau but these differences were not statistically significant. Researchers claimed that these results are unexpected in view of the functional adaptation observed in other musculoskeletal tissues, such as muscle and bone, in which a more obvious relationship with the magnitude of the applied mechanical stress has been observed. However, in this study, a high inter-individual variability of the mean and the maximal cartilage thickness values in all surfaces was observed, both in the triathletes and in the inactive volunteers. Functional adaptation of human joints to mechanical stimuli was again evaluated by comparing triathletes' and non-athletes' cartilage (Eckstein et al., 2002). They examined nine men and nine women triathletes, and 18 inactive healthy volunteers. Researchers reported that the knee joint cartilage thickness, and signal intensity were not significantly different between athletes and inactive volunteers, but male athletes displayed significantly larger knee joint surfaces. Female athletes displayed a significantly larger medial tibia and the difference in the total knee surface area reaching borderline significance. According to their findings Eckstein and his colleagues claimed that joint size can be modulated during growth, but the thickness of the cartilage does not adapt to mechanical stimulation.

In a cross sectional study, sports-related differences in biomarkers of bone resorption and cartilage degradation in endurance athletes were compared (O'Kane, Hutchinson, Atley, & Eyre 2006). Researchers asked whether differences in skeletal stresses in college athletes undergoing high-intensity training for diverse types of aerobic sports affect their skeletal metabolism. In this study, urinary cross-linked N-telopeptide (NTX) and urinary CTX-II were used as a bone resorption marker and as a cartilage degradation marker, respectively. 60 student athletes from crew, cross-country running, swimming and 16 non-athlete controls were participated in this study. Biomarker levels were compared after adjusted for BMI. NTX was highest in the rowers, and higher in rowers and runners than in swimmers or controls. CTX-II was significantly higher in runners than swimmers and controls, when adjusted for BMI. Researchers suggested that crew undergo the highest bone remodeling and runners the highest cartilage degradation. However, in a previous study no difference in the NTX concentrations among the high impact, medium impact and nonimpact sport groups were noted (Creighton, Morgan, Boardley, & Brolinson 2001).

Gratzke, Hudelmaier, Hitzl, Glaser, & Eckstein (2007) compared the morphologic characteristics of knee cartilage and muscle status of professional weight lifters and sprinters. Their hypothesis was subjects with high muscle strength display thicker knee cartilage and larger joint surface areas than nonathletic volunteers, and knee cartilage morphologic characteristics correlate more strongly with muscle force than with muscle cross-sectional areas. In this cross-sectional study seven weight lifters and seven bobsled sprinters were examined and compared with 14 adult nonathletic volunteers. Results showed that experimental group displayed significantly larger extensor muscle moments and cross-sectional areas. Also, patellar cartilage thickness of weight lifters and sprinters were larger than nonathletic volunteers but no significant differences in the cartilage thickness of the other knee joint cartilage plates or joint surface areas. Gratzke and collaborates claimed that cartilage thickness has much less ability, if any, to adapt to mechanical loading than muscle.

Investigations on acute effect of sport exercise on articular cartilage are a very new subject. First study according to our knowledge was performed by Eckstein et al., (1998). In this study, Eckstein and collaborates quantified the in vivo changes of cartilage volume and thickness with MRI after physical exercise. The patellae of eight volunteers were imaged six times at physical test by using a spoiled fat-suppressed gradient-echo sequence with an acquisition time of 4.10 minutes. The volunteers then performed 50 knee bends, and two more data sets were acquired 3-7 minutes and 8-12 minutes after exercise. According to the results, a statistically significant decrease in cartilage volume was observed 3-7 minutes (6.0%) and 8-12 minutes (5.2%) after exercise. They observed that the deformation was homogeneous throughout the joint surface. In 1999, Eckstein, Tieschky, Faber, Englmeier, & Reiser, analyzed the deformation, recovery, and fluid flow in human articular cartilage after dynamic loading. The patellae of seven volunteers were imaged at physical rest and after performing knee bends with MRI. Patellar cartilage deformation ranged from 2.4 to 8.6% after 50 knee bends, and from 2.4% to 8.5% after 100 knee bends. Analyses showed that repeated sets of dynamic exercise at intervals of 15 min did not cause further deformation. The rate of fluid flow during relaxation ranged from 1.1 to 3.5 mm^3/min and was highly correlated with the individual degree of deformation after knee bends. Latter year Eckstein, Lemberger, Stammberger, Englmeier, & Reiser, (2000) compared the effect of static and dynamic loading on patellar cartilage. They hypothesed that static loading (squatting at a 90 degrees angle) and dynamic loading (30 deep knee bends) cause different extents and patterns of patellar cartilage deformation. Twelve healthy volunteers were examined and the volume and thickness of the patellar cartilage determined before and from 90 to 320s after loading. Following knee bends, a residual reduction of the patellar cartilage volume (-5.9+/-2.1%) and of the maximal cartilage thickness (-2.8+/-2.6%) was calculated. Following squatting, the change of patellar cartilage volume was -4.7+/-1.6% and that of the maximal cartilage thickness -4.9+/-1.4%. Results demonstrated that the volume changes were significantly lower after squatting than after knee bends, but the maximal thickness changes higher.

Hohmann, Wörtler, & Imhoff, (2004) investigated whether external impact loading in marathon runners creates internal stresses on bone and cartilage that are demonstrable on MR images. In this study, six recreational and two semi-professional runners underwent MRI of the hip and knee before and after a marathon run. Results of this study suggested that the high impact forces in long-distance running are well tolerated and subsequently do not demonstrate changes on MR images, because the pre-run and post-run scans failed to demonstrate marrow oedema, periosteal stress reactions, or joint effusions in seven runners. However, only one patient who underwent a reconstruction of his anterior cruciate ligament 18 months ago demonstrated a small effusion in the reconstructed knee before and after the race. Articular cartilage subjected to the high repetitive loading cycles occurring during long-distance running and ability to remain intact is still the topic of controversy. Kessler, Glaser, Tittel, Reiser, & Imhoff, (2006) also, investigated the changes in cartilaginous volumes of the tibia, patella, and medial and lateral menisci after extreme dynamic loading as occurs in long-distance runners. 30 male athletes ran around a predetermined and precisely measured course (5, 10, 20 km). Overall, researchers observed significant reductions in volume for the patella, tibia, and menisci. Actual change was observed after a running distance of 5 km. However, other statistical reduction was observed only for medial meniscus after 10 and 20 km. On the basis of the results of this study, the authors assumed that the cartilage is able to adapt well to the loads caused by running.

In an extended report, Eckstein et al., (2006) evaluated the deformational behavior of patellar and femorotibial cartilage for different types of physiological activities and tested the hypothesis that in vivo deformation of cartilage is modified by intense physical exercise. Researchers analyzed the MR images to determine cartilage volume before and after physical activity (knee bends, squatting, normal gait, running, cycling) in the patella of 12 volunteers. Deformation of femorotibial cartilage was investigated in 10 participants (knee bends, static compression, high impact loading). Also, patellar cartilage deformation after knee bends was compared in seven professional weight lifters, seven sprinters, and 14 untrained volunteers. The highest patellar cartilage deformation was observed after knee bends (-5.9%) and the lowest after cycling (-4.5%). Tibial cartilage deformation was greatest under high impact loading (-7%), but small for other activities. Researchers did not find a significant difference between athletes and non-athletic controls. The findings provide no evidence that adult human cartilage properties are amendable to training effects in vivo.

Koo & Andriacchi (2007) compared the influence of global functional loads with local contact anatomy on articular cartilage thickness at the knee. Researchers isolated the relationship between cartilage thickness predicted by individual variations in contact surface geometry based on the radii of the femur and tibia vs. cartilage thickness predicted by individual variations in joint loading. Knee MR images and the peak knee adduction moments during walking were obtained from 11 young healthy male participants. Koo & Andriacchi realized that in general, pressure was higher in the lateral than medial compartments and cartilage was thicker in the lateral than medial compartments. Also, the peak knee adduction moment showed a significant positive linear correlation with medial to lateral thickness ratio in both femur and tibia. The results of this study suggested that the dynamics of walking is an important factor to describe individual differences in cartilage thickness for normal participants.

It is still unclear whether long-distance running has a deleterious effect on joint health; therefore Kessler, Glaser, Tittel, Reiser, & Imhoff, (2008) examined the rate of recovery from alterations occurring at the knee joint in marathon runners. Researchers hypothesized that tibial, patellar, and meniscal cartilaginous volumes are able to recover adequately from changes due to repeated loading immediately after cessation. Cartilaginous volume was measured by MRI before and immediately after the 20 km run and after a recovery period of 1 hour. Results showed that there was a significant decrease in cartilage volume after the 20-km run. After 1 hour of rest, no significant reduction of cartilage volume was measured for any sides of knee cartilage. However, the values recorded for the menisci were borderline, which indicates that recovery of meniscus volume lags behind that of articular cartilage. Researchers indicated that a clear tendency toward rapid recovery of the cartilaginous and meniscal volumes at the knee. The results of this study lead to the assumption that the cartilage and the menisci are well able to adapt to the loads caused by running and the articular structures recover rapidly so that exercise could be continued after a short time without reservation.

Effect of exercise on the biomarkers of cartilage deformation or bone turnover are relatively new topics in literature. Kersting, Stubendorff, Schmidt, & Brüggemann, (2005) investigate the relationship between running induced joint loading at the knee, changes in cartilage volume and serum COMP concentration. In this study, serum COMP levels and knee cartilage volumes of experienced runners were tested before and after running and joint loading was determined using a biomechanical model of the lower extremity. Blood samples and magnetic resonance imaging scans were taken before and following a 1h training run. Also, researchers calculated individual knee joint loading parameters from positional data and ground reaction forces. According to this results, Kersting and collaborates explained that changes in cartilage volume and COMP showed significant correlations. However, net joint forces did not explain the differences in cartilage changes. Kersting and collaborates found significant difference in serum COMP concentration after 1 hour of running training. Mundermann, Dyrby, Andriacchi, & King, (2005) tested the hypothesis that physiological cyclic loading during a 30-min walking exercise causes an increase in COMP. In their study amount of exercise impact on knee joint and volume of exercise is absolutely lower than Kersting's study. Also, Mundermann and collaborates' participants were 10 health non-athletes. Blood samples were drawn immediately before and after, and 0.5h, 1.5h, 3.5h and 5.5h after a 30-min walking exercise. On a separate day, blood samples were drawn from the same 10 participants during 6h while they were resting on a chair. Researchers compared serum COMP concentrations within the exercise protocol and within the resting protocol. Mundermann and colleagues observed a significant increase immediately after the walking exercise. Their study showed that even a moderate walking activity can significantly influence serum COMP concentration and the immediate response points to a diffusion time of COMP fragments from cartilage to the blood of 30 min or less.

After the evaluation of 30 and 60 minutes of exercise on articular cartilage, Kim, Lee, & Kim (2007) evaluated muscle and cartilage biomarkers and cytokine secretion during an ultra-marathon (200 km running). Venous blood samples were taken before, midway and immediately after the race from 54 trained male ultra-marathon runners. In this study, COMP was used to determine cartilage damage. Serum COMP concentration increased 1.3 fold at 100 km and 3-fold at the end of 200 km. According to results, ultra-marathon running clearly has a major impact on muscle and cartilage structures. Researchers concluded that ultra-long running causes a wide range of injury-related changes and that possibly greater damage occurs in the latter half of the race. Two years later, again Kim, Lee, & Kim (2009) compared muscle and cartilage damage after a marathon (42.195 km) and an ultra-marathon (200 km). Twenty male marathoners and ultra-marathoners participated in their study. Serum COMP level was increased 1.6-fold at 10 km during a marathon race and stayed constant up to end of the marathon. This level was significantly decreased at first day and declined to the pre-race level after 2 days recovery. However, serum COMP was increased 1.9-fold after a 200-km race and returned to the pre-race level on day 6. These findings demonstrated that running distance may affect on the impact-stress related damage in cartilage. Also researchers stated that running distance and the tissue type may affect the required time for recovery.

Recently, Niehoff et al. (2008) tested the hypothesis that elevation of serum COMP level depends on loading mode of physical activity. In their study, researchers investigated whether there is a relationship between the mode of physical activity and COMP concentration and whether the lymphatic system contributes directly or indirectly to the rise in serum COMP concentration. Only five male participants were enrolled in this study. Blood samples were taken before, after and at seven time points within 1 hour after three different loading interventions of 30 min duration or on a day of complete rest. The interventions were running, slow knee bends and lymph drainage, which is a delicate form of massage that stimulates the body’s lymphatic system. Results showed that 30 minutes running exercise significantly increased the serum COMP concentration and this level stayed constant up to 1h following the exercise. However, slow knee bends and lymphatic drainage had no effect on the serum COMP concentration. According to these findings, it was concluded that impact-loading results in a greater exudation of COMP from the joint cartilage.

There are some studies about the effect of different interventions on the articular cartilage in literature, but the number of these studies is very limited. In a community rehabilitation program, Lin, Davey, & Cochrane (2004) mentioned the effectiveness of water based exercise program on the knee-hip osteoarthritis. In this study, sixty-six participants were offered a water-exercise program and forty participants received monthly education material and quarterly telephone calls. Effectiveness of interventions was evaluated with

WOMAC and physical function tests. Post-test results indicated that there was a significant improvement in physical function and reduction in the perception of pain of exercise group. This study showed us that 12 months of community-based water exercise of elderly people with knee/hip osteoarthritis improves physical function, general mobility and flexibility. Roos & Dahlberg (2005) mentioned about the positive effects of moderate exercise on knee cartilage in patients at risk of osteoarthritis. In their study, Ross & Dahlberg evaluated the effects of moderate exercise on glycosaminoglycan content in knee cartilage in subjects at high risk of knee osteoarthritis. Forty-five participants were randomly assigned to supervise exercising group for 3 times weekly for 4 months or to control group. According to researchers, patients at risk of knee osteoarthritis who begin exercising indicated that adult human articular cartilage has a potential to adapt to loading change. Remarkable finding of this study was that supervised exercise may be a good treatment not only to improve joint symptoms and function, but also to improve the knee cartilage glycosaminoglycan content in patients at high risk of developing osteoarthritis.

Serum levels of COMP concentration increase temporarily after physical exercise also in patients with knee osteoarthritis (Andersson et al., 2006). They monitored serum COMP concentration of patients of knee osteoarthritis during a physical exercise or rest. Andersson and his collaborates collected blood samples from training and control groups before and after exercise or rest. Participants performed one-hour supervised exercise twice a week and daily home exercises for six weeks. Also in supplementary study 7 individuals were subjected to the same exercise program and sampling of blood was performed at fixed intervals before, immediately after, 30 and 60 minutes after the exercise session and then with 60 minutes interval for another five hours after exercise to monitor the short-term changes of serum COMP concentration. Serum

COMP levels of participants were not significantly different at the beginning of the study. 60 minutes exercise caused a significant increase in serum COMP levels and after 60 minutes of rest, serum COMP levels decreased in both groups. Results also indicated that median serum COMP values in samples obtained prior to exercise or rest at baseline and after 24 weeks did not change between start and end of the study. Similar to Mundermann's (2005) findings serum COMP was increased immediately after exercise and decreased to baseline levels after 30 minutes rest. According to the results, researchers suggested that samples of blood for analysis of serum COMP should be drawn after at least 30 minutes rest in a seated position. And no increase was seen after a six-week exercise program which is interpreted as any effect of individualized supervised exercise on cartilage turnover is permanent.

In a longitudinal study, Foley, Ding, Cicuttini, & Jones, (2007) evaluated the physical activity and knee structural changes in adult males and females. In this study, 325 subjects were measured at baseline and approximately two years later. Measured parameters of this study were physical activity questionnaire, physical work capacity, lower-limb muscle strength, knee cartilage volume, tibial plateau area and cartilage defect score. Results of this study indicated that physical load stimulates the knee cartilage volume and tibial plateau area so that they are interpreted as dynamic structures. Remarkable comment of researchers was that physical activity may have both good and bad effects on the knee, because, greater muscle strength and endurance fitness may be protective against cartilage loss, but it also may result in a maladaptive enlargement of subchondral bone in both sexes. Effect of physical activity on articular knee joint structures was evaluated also in a community-based study (Racunica et al., 2007). Racunica and collaborates examined the association between intensity, frequency, and duration of physical activity and knee structures. 297 healthy adults without knee injury history participated in this study. Tibial cartilage volume, tibiofemoral cartilage defects, and bone marrow lesions of the participants were measured. Physical activity and anthropometric data of the participants were followed via questionnaire about ten year. Results revealed that tibial cartilage volume increased with frequency and duration of vigorous activity reported 10 years previously, as well as recent vigorous activity in the 7 days prior to MRI. Recent weight-bearing vigorous activity increased with tibial cartilage volume and was inversely associated with cartilage defects. A reduced risk of bone marrow lesions was associated with regular walking. These findings showed that vigorous physical activity appears to have a beneficial effect on knee articular cartilage in healthy, community-based adults with no history of knee injury or disease. Also it is suggested that physical activity is good for the heart is also good for the knees.

In a cohort study of healthy middle-aged women, Wijayaratne et al., (2008) searched the determinants of change in patella cartilage volume over two years among healthy middle-aged women with no clinical knee osteoarthritis. MRI of one hundred and forty-eight women was performed at baseline and at 2nd year, to assess patella cartilage and bone volume. Self-reported exercise questionnaire was used to assess exercise content. Results showed that participation in exercise associated with a reduced rate of patella cartilage volume loss. Researchers concluded that increased patella bone volume and exercise participation tends to be associated with a reduction in the rate of patella cartilage volume loss.

In addition to studies about the effect of exercise on cartilage markers, Lester et al. (2009) investigated the influence of exercise mode bone biomarker responses. According to Lester and collaborates, in rodents, an osteogenic index has been used to predict the osteogenic potential of exercise but has not been established in humans. Sixty-nine young, healthy college women were enrolled in this study. Participants were divided into four groups aerobic, resistance, combined aerobic and resistance and control group and trained for eight weeks. Researchers collected serum biomarkers and BMD before, during and after eight weeks of training. Small changes in volumetric and areal BMD were observed in the distal tibia in the aerobic and combined groups however, researchers could not find a difference in CTX-I concentrations. Researchers reported that serum CTX-I concentrations were similar in all four groups pre-training and remained stable throughout the training programs.

Some research groups published review articles about the effect of exercise on articular cartilage but still there is no consensus about the deformation and adaptation of articular cartilage to physical exercise. Initially, Eckstein, Hudelmaier, & Putz, (2006) published a review about the effects of exercise on human articular cartilage. In this review Eckstein and collaborates summarized researches on short-term (deformational behavior) and long-term (functional adaptation) effects of exercise on human articular cartilage. They explained that human cartilage deforms very little in vivo during physiological activities and recovers from deformation within 90 min after loading. As mentioned before, Eckstein indicated that cartilage undergoes some type of atrophy (thinning) under reduced loading conditions, such as with postoperative immobilization and paraplegia. They claimed that in contrast to findings about reduced loading, increased loading is not associated with increased average cartilage thickness. However, in a very recent review, Hunter & Eckstein, (2009) mentioned about the benefits of exercise on weight control, disease management advantages for cardiovascular disease and diabetes, in addition to improving psychological well-being amongst an array of other benefits. Researchers indicated a community perception that exercise is potentially deleterious to one's joints. However, researchers indicated that in the absence of joint injury there is no evidence to support for the common misconception that exercise is deleterious to one's joints. They concluded that exercise has positive salutary benefits for joint tissues in addition to its other health benefits.

CHAPTER 3

MATERIALS AND METHODS

This study was designed to determine if deformational behavior and functional adaptation of articular cartilage are changed by moderate amount of high-impact, impact or non-impact physical exercise programs. The chapter begins with the (1) Overall Design of the Study, and covers (2) Participants, (3) Interventions (4) Physical and Physiological Measurements, (5) Blood Tests, and (6) Statistical Analysis.

3.1 Overall Research Design

A Randomized Control Trial study design where comparison of four groups, consisting of 12 participants each, was selected for this study. The design was chosen to examine the possible differences among four groups of participants in terms of deformational behavior and functional adaptation of articular cartilage (Figure 2).

At the beginning and the end of the study, each participant participated a serious of tests. All the tests were performed in the laboratories of the Middle East Technical University at Ankara. These tests composed of physical and physiological tests, knee exercise and blood collection tests. This blood samples were analyzed in a biochemistry laboratory and determined the level of biochemical markers of cartilage or bone degradation. Significance of changes was compared by statistical methods.

3.2 Participants

48 male students from various departments of the Middle East Technical University and aged between 19-25 years (M_{age} = 21.8, SD= 1.9) were participated in this study. Participants were voluntarily enrolled in this study. 36 of the participants were randomly assigned to exercise groups whereas remaining participants (n=12) recruited as a control group. To meet the requirements of the study, participants had to be healthy males with a sedentary life style who had no regular exercise backgrounds but had intermediate level swimming and cycling experience. Availability of participants for the tests and appropriateness of the schedule of the exercises for students were other major inclusion criteria. Criteria for exclusion were: osteoarthritis, rheumatoid arthritis or other inflammatory joint disease, knee arthroplasty intra-articular steroid injection malalignment of the knees (varus/valgus) larger than 15 °, recent (6 months) fracture of lower extremity, lack of understanding of the study (dementia, language problems), and abuse of drugs or alcohol. Also, students from physical education and sports department were not accepted to this study. During intervention period 2 participants were excluded from the study because of the health problems. Also 2 participants were excluded from the study at biochemical analyses. The exact nature of the studies' aim was explained to each voluntary participant and written consent and protocol of the study was approved by the Ethical Comity.

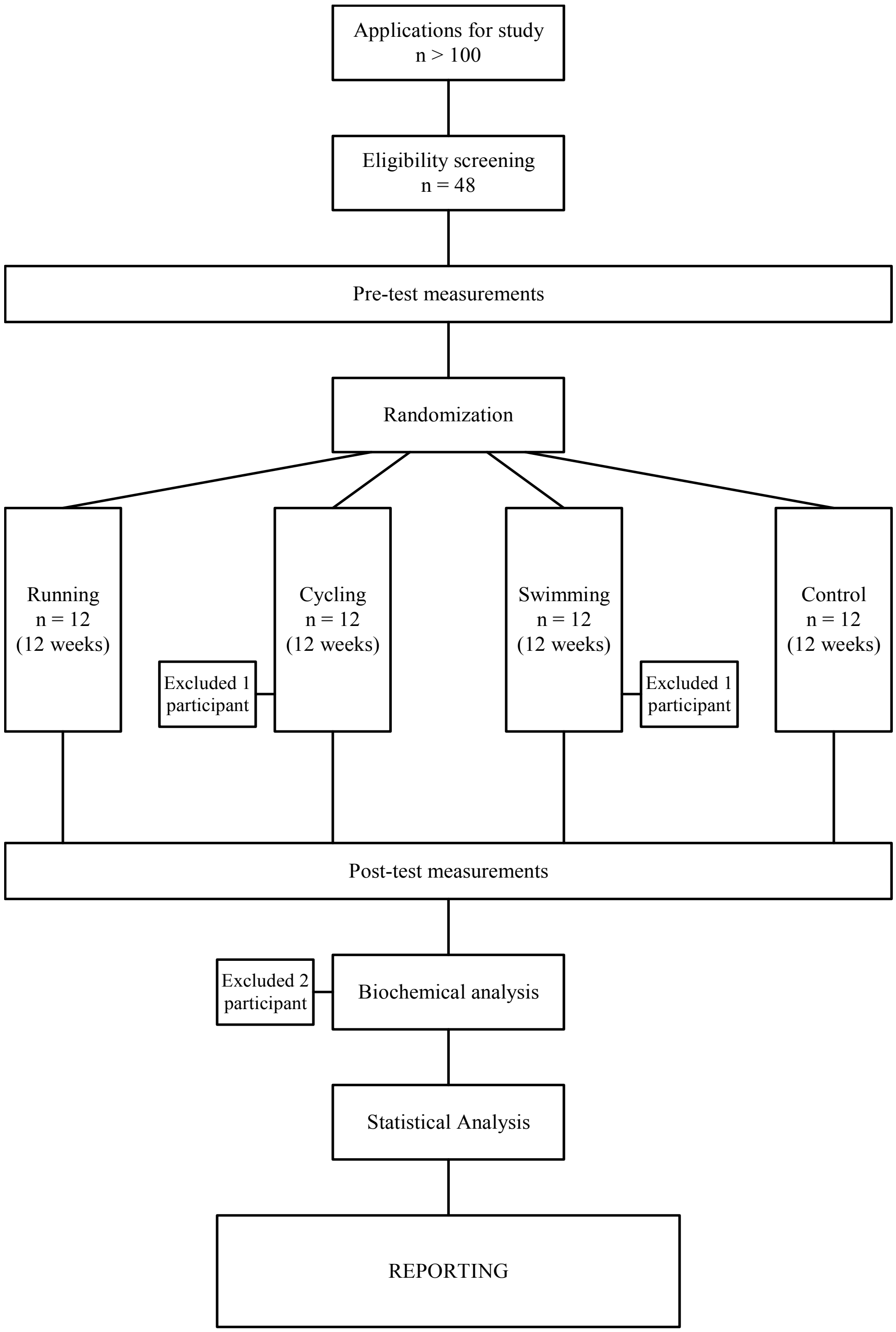


Figure 2.Flow chart of research design.

3.3 Interventions

At the beginning and the end of the study, each participant took part in a serious of tests. These tests were moderate intensity walking tests for blood sampling, isokinetic leg strength measurements, VO_2max measurements, Body Mass Index (BMI) measurements.

After first measurements, participants were randomly and equally assigned to swimming (n=12), running (n=12), cycling (n=12) and control groups (n=12). All exercise groups participated in sessions of 40 minutes per day, 3 days per week for 12 weeks. Each session started with a 5 minute warm-up, continued with a main set for 30 minutes at their individual target heart rate zone (60-70 % of heart rate reserve) and finished with a 5 min. cool down period (Figure 3). The individual target heart rate was determined according to the American College of Sport Medicine's (ACSM) Guidelines for Exercise Testing and Prescription (ACSM, 2001). Rather than skill acquisition volume and intensity of exercise were emphasized in all exercise groups. Swimming exercises were composed of front crawl swimming and kicking drills. All participants in swimming group had at least intermediate level experience and during main sets they performed swimming skills in a random manner at their individual heart rate zone. Cyclers had to continue exercise between 60-80 RPM and resistance of cycle ergometers (Monark E 834) were adjusted individually to keep each participant in his target heart rate zone. Participants in the running group performed sessions on the treadmill (Quinton Q65) with 1.5 % incline and speed of the treadmill was determined according to individual heart rate zone. Throughout the 12 weeks Heart Rate Reserve (HRR) were held constant (60-70%) while speed of the exercises was increased according to individual progression. The target heart rate zone was determined by the Karvonen formula (Bompa, 1999, p.87).

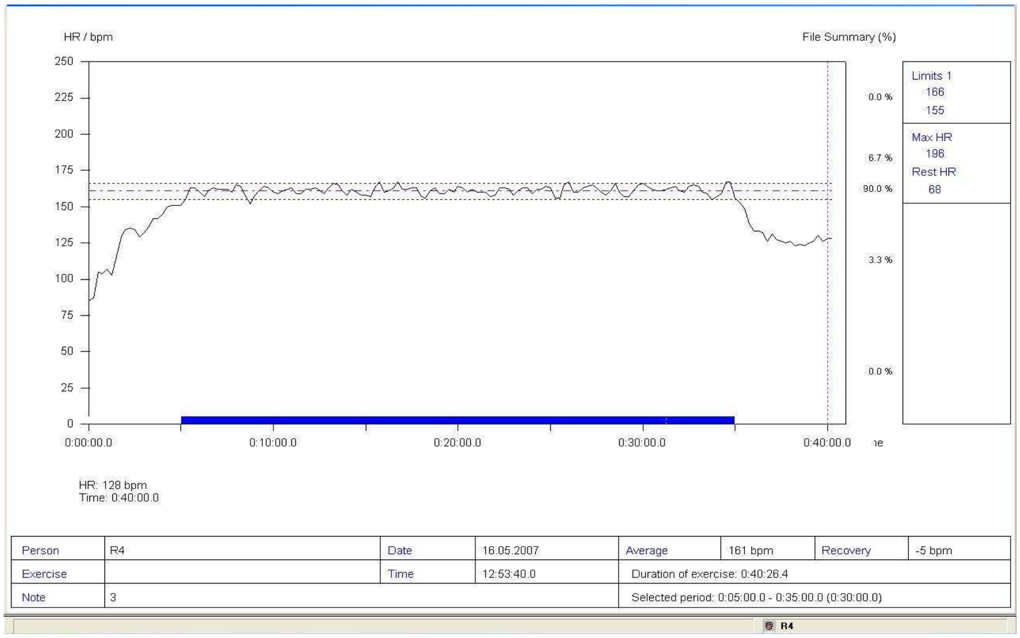


Figure 3. A sample of heart rate during a training session.

Participants in the running and cycling groups attended sessions in the human performance laboratory one by one, three times a week throughout their weekly schedule. This was every Monday, Wednesday and Friday as determined by the instructor. The swimming group performed exercise sessions in the indoor swimming pool according to the similar schedule at Tuesdays, Thursdays and Saturdays. The heart rate of the participants was measured and stored by heart rate monitors (Polar, Vantage NV Heart Rate Monitor) during exercise sessions. Throughout the 12-week period, the control group was told not to participate in any organized or structured exercise and to continue their daily life activities.

3.4 Physical and Physiological Measurements

3.4.1 Body Mass Index (BMI)

BMI is the ratio of body weight to height squired (Heyward & Stolarczyk 1996). To calculate BMI, the body weight was measured in kilograms by Seca 767 electronic column scale (Seca gmbh & co. Hamburg, Germany) and the height was measured by Harpenden Stadiometer (Holtain ltd. Crosswell, United Kingdom) and converted from centimeters to meters (cm/100).

3.4.2 Endurance (VO_2max) Measurements

In this study, VO_2max was measured by performing standard Bruce Protocol (Bruce, Kusumi & Hosmer 1973) on a Jager LE 200 CE treadmill. The exercise workloads gradually progressed in increments from moderate to maximal intensity. In particular, the Bruce-Protocol has a very low start speed, but a large incline (10 %). The speed and incline were increased simultaneously every third minute (Fredriksen, Ingjer, Nystad & Taulow, 1998). The participants were considered to have reached their VO_2max if maximal heart rate was reached, Rating of Perceived Exertion (RPE) were reached to 17 or more and attainment of a respiratory exchange ratio of 1.15 or greater. Oxygen uptake was calculated from measures of oxygen and carbon dioxide in the expired air and minute ventilation, and the maximal level was determined at or near test completion. Measurements were performed with VIASYS Healthcare ergospirometry line, the MasterScreen CPX (Wuerzburg, Germany). Results were presented as ml/kg/min (mililiters of oxygen per kilogram of body weight per minute).

3.4.3 Isokinetic Strength Measurements

Isokinetic strength data were recorded with the Biodex System Dynamometer (Biodex Medical Inc, Shirley, NY) to assess strength of the quadriceps and hamstrings muscle groups. Participants were placed in a comfortable upright-seated position on the Biodex dynamometer chair and was secured using thigh, pelvis and torso straps in order to minimize extraneous body movements. The lateral femoral epicondyle was used as the bony landmark for matching the axis of rotation of the knee joint with the axis rotation of the dynamometer resistance adapter. The participants were placed in a position that allowed for a comfortable and unrestricted motion of knee extension and flexion from a position of 90 degrees of flexion to terminal extension. Gravity correction was obtained by measuring the torque exerted on the dynamometer resistance adapter with the knee in a relaxed state at terminal extension. Values for the isokinetic variables measured were automatically adjusted for gravity for the Biodex Advantage Software Rev. 3.27.

Before the measurements of physical performance, the participants warmed up on a bicycle ergometer for 5 minutes and then stretched their body parts. Before the test trials, participants were instructed to perform their maximum efforts and participants did five isokinetic concentric knee flexion and extension at 60^{o}/sec with their dominant limbs. The dominant leg was defined as the preferred kicking leg. Peak torque to body weight (PT/BW) was chosen for strength measures.

3.5 Blood Tests

3.5.1 Blood Sampling

Blood obtaining procedures were modified from Mundermann (2005). Participants were asked to limit their physical activity 48 h prior to the experiment. On the day of the experiment, participants consumed breakfast within 1 h of waking, and the experiment started within 3-4 h of waking. Participants were seated on a chair for 15 min immediately before the experiment. Five-milliliter blood samples were drawn by a certified research nurse from the same antecubital vein immediately before, immediately after, and 0.5 h, after a 30-min walking exercise. Participants consumed lunch immediately following the 1.5-h blood draw. During the walking exercise of the test protocol, participants walked at the pace of 5 km/h with 1.5 % grade on treadmill. After walking exercise participants sat on an office chair for 30-min and were asked to perform a minimal amount of physical activity. By this procedure blood samples were taken at rested, degenerated and regenerated state of the knee cartilage.

Blood sample collection and storage procedures were done as described previously (Andersson et al, 2006). Venous blood samples were obtained from vena mediana cubitii. After clotting for 60 min at room temperature, they were centrifuged at 5000 rpm for 10 minutes. The serum samples were stored at -20°C until all the serum samples were obtained. The samples were then stored at -80°C for long-term storage until analysis. General procedure of blood sampling is tabulated at figure 4.

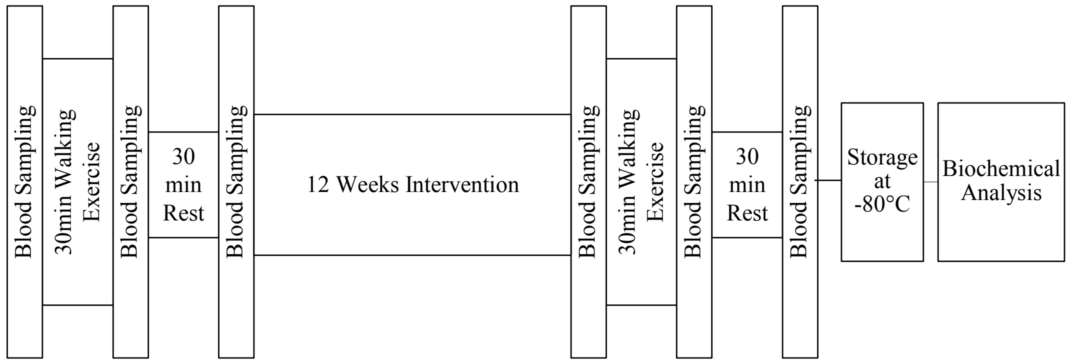


Figure 4. Design of Blood Sampling

3.5.2 Biochemical Analysis of the Blood Samples. Enzyme-Linked Immuno-sorbent Assay (ELISA)

Serum COMP and CTX-I levels were analyzed with a sandwich-ELISA (COMP® ELISA; AnaMar Medical AB, Lund, Sweden) and (Serum CrossLaps® ELISA; Immunodiagnostic Systems Nordic A/S, Herlev, Denmark) respectively.

According to manufacturers, principle of the procedure for COMP ELISA is:

> In the competitive COMP ELISA, bovine COMP is used to coat the microtiterplates and serum from rats as calibrators. A polyclonal antisera directed against COMP from rats is used as the primary antibody and is incubated together with samples and calibrators directly in the microtiterplate. After the wash a secondary antibody is added to the well. The plate is incubated, developed and read at 450 nm. The response is inversely proportional to the concentration of Animal COMP in the sample.

And principle of the procedure for CTX-I ELISA (2008) is:

> The Serum CrossLaps® ELISA is based on two highly specific monoclonal antibodies against the aminoacid sequence of EKAHD-ß-GGR, where the aspartic acid residue (D) is ß-isomerized. In order to obtaina specifi c signal in the Serum CrossLaps® ELISA, two chains of

> EKAHD-ß-GGR must be cross linked. Standards, control, or unknown serum samples are pipetted into the appropriate microtitre wells coated with streptavidin, followed by application of a mixture of a biotinylated antibody and a peroxidase conjugated antibody. Then, a complex between CrossLaps antigens, biotinylated antibody and peroxidase conjugated antibody is generated, and this complex binds to the streptavidin surface via the biotinylated antibody. Following the one step incubation at room temperature, the wells are emptied andwashed. A chromogenic substrate is added and the colour reaction is stopped with sulfuric acid. Finally, the absorbance is measured.

All ELISA analysis was performed in a private institution and assay procedures were followed according to the manufacturers' guidelines.

3.6 Statistical Analyses

The statistical analysis were performed using the computer program SPSS. The data were analyzed with separate 4x2 (groups and time) mixed repeated-measures ANOVA design with kinetic, isokinetic, explosive leg power, and proprioceptive sense values as the dependent measures. Separate analyses of variances was chosen because all of the dependent variables are of autonomous interest.

Bonferroni-adjusted paired-samples t-tests were employed for post-hoc analyses. A corrected p-value, which was $p = .05$ divided by number of comparisons for each dependent variable, was thus employed. All cross-evaluations of blood samples were tabulated at figure 5.

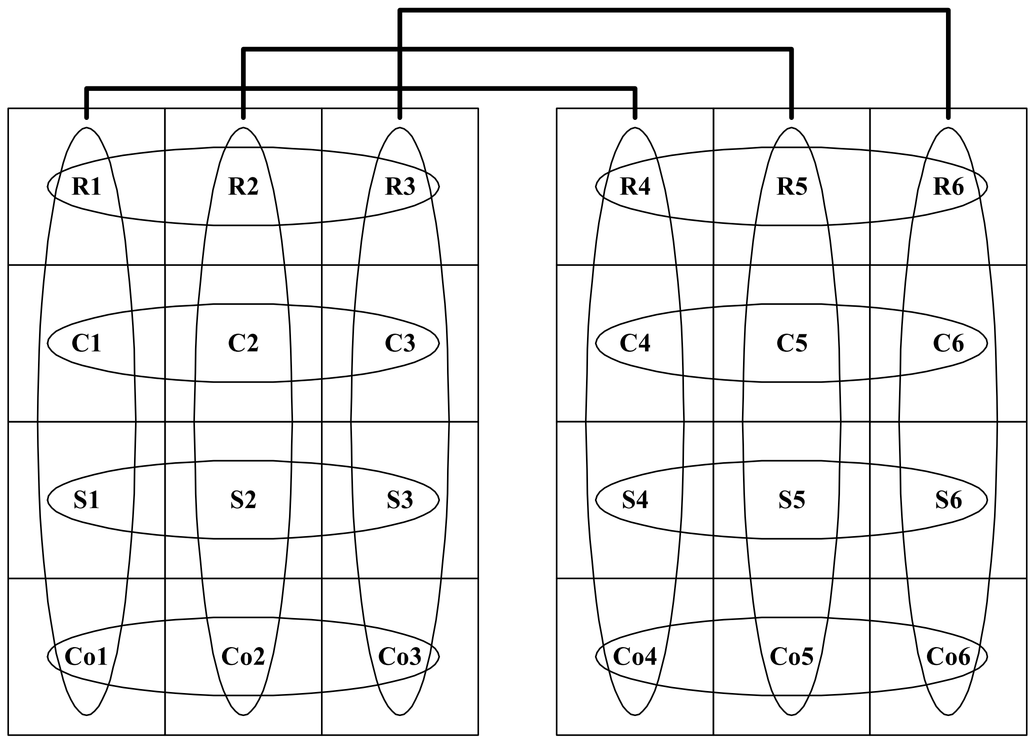


Figure 5. Multivariate and Univariate Comparisons of Blood Samples.

CHAPTER 4

RESULTS

This chapter, which was divided into three main sections, presents the results of the study. The first section, describing the demographic information and physiological adaptation of the participants, is the non-hypothesized part of the study. The second section provides data related with the serum COMP concentrations. And the last section includes results related with the serum CTX-I concentration.

4.1 Demographic Information of the Participants

4.1.1 Participants

Descriptive information of participant's was gathered at the beginning of the study. Statistically significant differences were not observed among the running, cycling, swimming and control groups' age, height and BMI at the pre-test measurements (Table 1).

Table 1. Physical characteristics of participants

		N #	Age (yrs)	Height (m)	Weight (kg)	BMI (kg/m^2)
	Running	11	20.7±1.3	1.77±.1	72.6±9.0	23.1±2.0
	Cycling	11	21.1±1.5	1.79±.1	71.0±8.3	22.1±2.7
Groups	**Swimming**	11	22.8±1.9	1.75±.1	75.2±8.3	24.7±2.8
	Control	11	22.6±2.1	1.78±.1	74.6±4.0	23.7±1.3
	Total	44	21.8±1.9	1.77±.1	73.4±7.6	23.4±2.4

During the implementation period 32 training sessions were performed. Specifically participation rates of participants in running, cycling and swimming groups were 86%, 84% and 90%, respectively.

4.1.2 Body Mass Index

The results of this study showed that running, cycling or swimming exercises of 40 minutes per day, 3 days per week for 12 weeks resulted in a significant decrease in Body Mass Index.

Multivariate analysis showed that there was no significant main effect for BMI measurement for Group ($F (1,40) = 2.41$, $p > .05$, Eta-squared (η^2) = .15) or Time by Group interactions ($F (3,40) = 1.18$, $p > .05$, $\eta^2 = .08$). Significant ($F (1,40) = 20.24$, $p < .05$) main effect ($\eta^2 = .34$) for Time however was obtained. Body mass index decreased significantly in all exercising groups.

Based on multivariate analysis, it is only possible to examine the main effect for the Time variable, a within-subjects factor. An overall change in BMI of all participants was observed from pre-test to post-test via multivariate analysis. However, in order to find out which group changed significantly, a univariate simple effect analysis was performed for the time within level of treatment by using a syntax command in SPSS. Simple effect analysis showed that BMI of the participants decreased significantly with time in the running, the cycling and the swimming groups (Table 2).

Table 2. Simple Effect Analysis of Time for BMI

Groups	**DF**	**F**	**p**
Running	1	9.6	.00
Cycling	1	4.3	.05
Swimming	1	9.3	.00
Control	1	.6	.44

BMI results indicated that the mean body fat percent was 23.1±2.0 in the running group, 22.1±2.7 in the cycling group, 24.7±2.8 in the swimming group and 23.7±1.3 in the control group at pre-tests. At the post-test measurements, body fat percents decreased 3.2 %, 2.2 %, 2.9 %, 0.8 %, respectively and became 22.3±2.0, 21.6±2.4, 24.0±3.1, 23.5±1.5. Difference in body fat percentage between pre- and post-test was given in Figure 6.

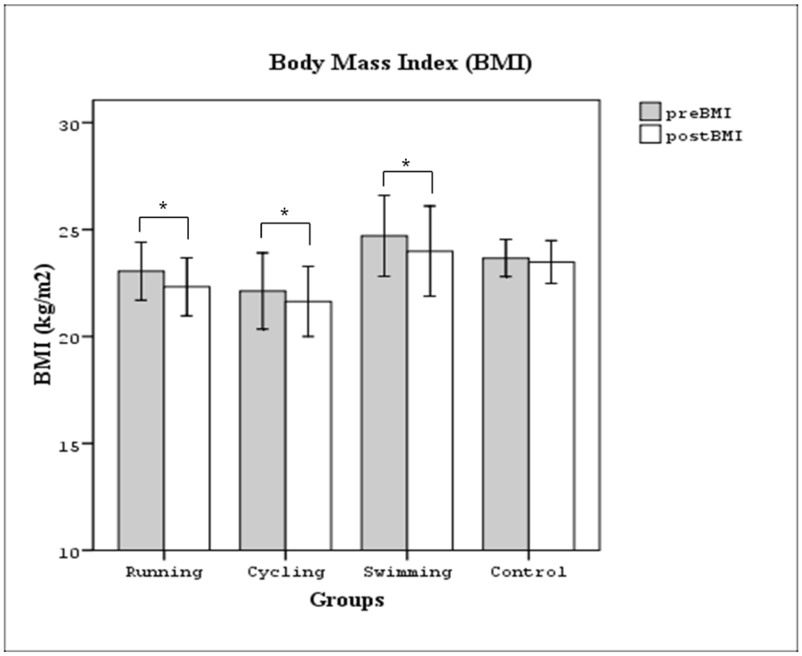


Figure 6. Body Mass Index Differences (p < .025).

4.1.3 Endurance (VO_2max) Measurements

VO_2max measurements showed that running, cycling or swimming exercises increased maximum oxygen consumption capacities of participants significantly. However, there was no significant difference in VO_2max values of control participants.

Multivariate analysis showed that there was no significant main effect for VO_2max measurement for Group ($F(1,40) = .08$, $p > .05$, $\eta^2 = .01$). Meanwhile, significant Time by Group interactions ($F(3,40) = 5.07$, $p < .05$, $\eta^2 = .28$) and significant main effect for Time ($F(1,40) = 66.70$, $p < .05$, $\eta^2 = .63$) was obtained. VO_2max, in other words endurance of the participants was increased significantly with the 12 weeks regular exercises in all experimental groups (Table 3).

Table 3. Simple Effect Analysis of Time for VO_2max

Groups	DF	F	p
Running	1	31.0	.00
Cycling	1	11.0	.00
Swimming	1	38.4	.00
Control	1	1.6	.22

VO_2max results indicated that the mean maximum oxygen consumption was 46.2±3.4 in the running group, 47.1±5.1 in the cycling group, 45.6±3.8 in the swimming group, and 47.3±3.6 in the control group at pre-tests. Percent decreases between pre- and post-test measurements for VO_2max were 10.6%, 6.2%, 12.0%, 2.3 %, respectively and became 51.1±5,8, 50.0±4,9, 51.1±4.3, 48.4±3.6. Difference between pre- and post-tests was given at Figure 7.

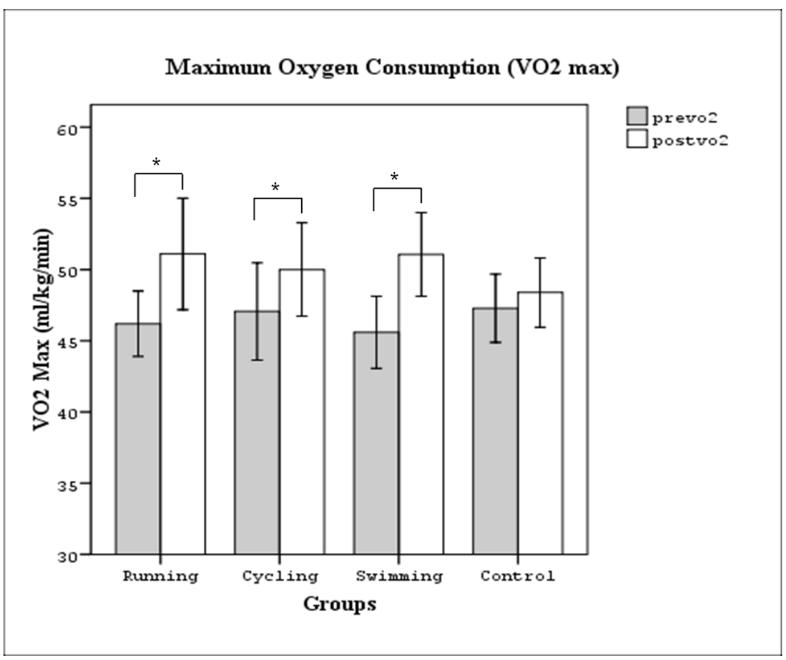


Figure 7. Maximum Oxygen Consumption Differences (p < .025).

4.1.4 *Isokinetic Strength Measurements*

The relative isokinetic strength of the dominant leg during extension did not increase significantly in running, cycling and control groups. There was, however, a significant increase in the swimming groups' strength due to 3 times a week swimming exercise.

Multivariate analysis showed that there was no significant main effect for the dominant quadriceps PT/BW for the group variable ($F(1,40) = 1.38$, $p > .05$, $\eta^2 = .09$) or the time variable by group interactions ($F(3,40) = .42$, $p > .05$, $\eta^2 = .03$). Meanwhile, significant main effect for Time was obtained, $F(1,40) = 7.01$, $p < .05$, ($\eta^2 = .15$). Dominant quadriceps PT/BW was just significant only at the swimming group (Table 4).

Table 4. Simple Effect Analysis of Dominant quadriceps PT/BW

Groups	DF	F	p
Running	1	.7	.42
Cycling	1	2.8	.10
Swimming	1	4.2	.05
Control	1	.6	.46

Isokinetic strength measurement results indicated that the mean dominant quadriceps PT/BW results were 298.1±48.6 in the running group, 279.3±31.9 in the cycling group, 266.0±27.7 in the swimming group, and 277.2±39.2 in the control group at pre-tests. Percent decreases between pre- and post-test measurements for relative strength were 2.3%, 5.1%, 6.6%, 2.3%, respectively and became 305.1±44.5, 293.6±32.4, 283.4±23.9, 283.5±29.5. Difference in isokinetic strength between pre- and post-tests was given at (Figure 8).

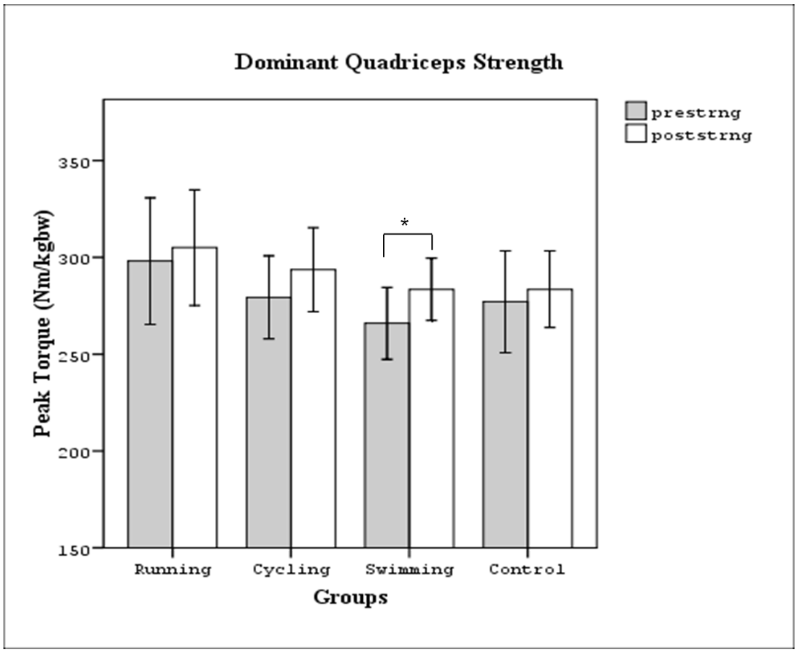


Figure 8. Dominant Legs, Quadriceps Strength Differences ($p < .025$).

4.2 Serum COMP Concentration Measurements

During pre- and post-test measurements, serum samples were taken at the recovery, the fatigue and the regeneration phases. Descriptive statistics of Serum COMP concentrations are presented in Tables 5 and 6.

Table 5. Pre-test Serum COMP concentrations (U/l)

	Recovery (M±SD)	**Fatigue** (M±SD)	**Regeneration** (M±SD)
Running (N=11)	10.07±1.8	12.93±2.9	10.71±2.2
Cycling (N=11)	9.74±2.3	12.39±1.9	11.00±1.9
Swimming (N=11)	9.68±1.6	12.42±1.8	10.99±1.4
Control (N=11)	9.49±1.4	12.52±1.1	10.54±1.4

Table 6. Post-test Serum COMP concentrations (U/l)

	Recovery (M±SD)	**Fatigue** (M±SD)	**Regeneration** (M±SD)
Running (N=11)	9.76±1.6	11.34±2.6	10.32±1.8
Cycling (N=11)	9.44±2.4	11.86±1.7	10.32±2.1
Swimming (N=11)	9.35±1.5	12.23±1.3	10.34±1.5
Control (N=11)	9.66±1.3	12.41±1.1	10.52±1.3

4.2.1 Serum COMP level differences among groups at pre- and post-test measurements

During pre-test measurements, serum COMP concentrations at the recovery state were not significantly different among groups. Similarly, there were no significant differences among groups after the 30 minute walking exercise. For the regeneration period, the same consistency was also valid. Main effect for group variable at the recovery state ($F\ (3,40) = .19$, $p = .90$), at the fatigue state ($F\ (3,40) = .17$, $p = .92$) or at the regeneration state ($F\ (3,40) = .18$, $p = .91$) is presented at Figure 9.

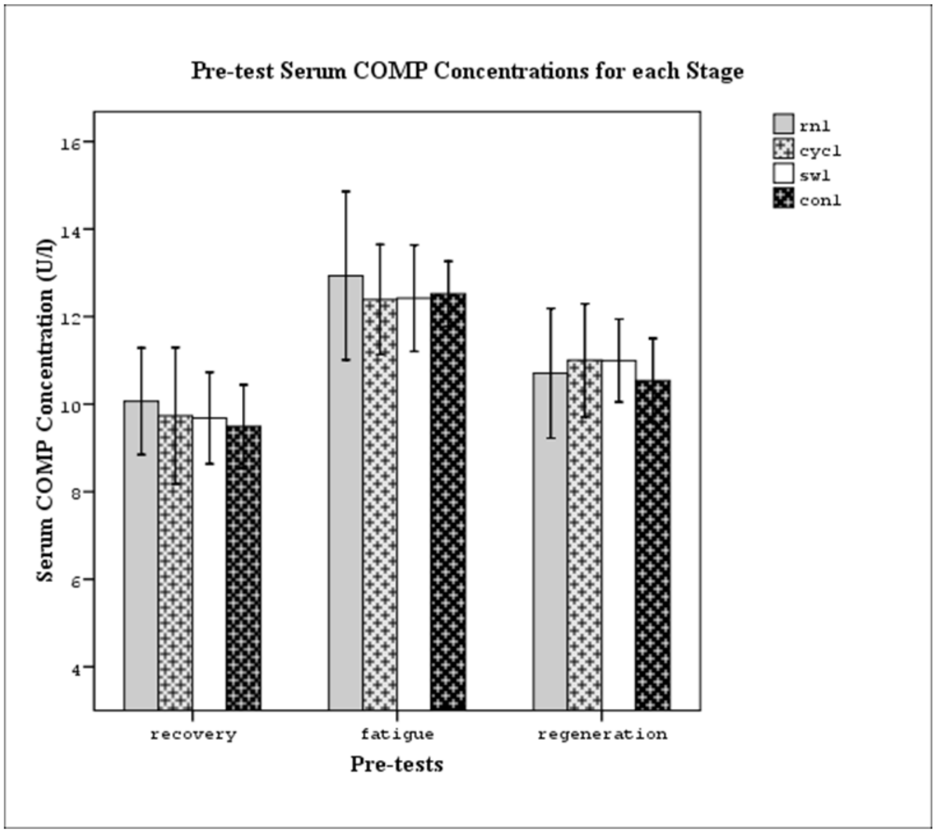


Figure 9. Serum COMP concentrations at different states during pre-test measurements.

Similar findings were also observed during post-test measurements. Serum COMP concentrations at the recovery state, after 30 minutes walking exercise and at regeneration were not significantly different among groups. Serum COMP concentration results showed no significant main effect for group variable during post-test measurements at the recovery state ($F(3,40) = .13$, $p = .99$), at the fatigue state ($F(3,40) = .79$, $p = .51$) or at the regeneration state ($F(3,40) = .04$, $p = .99$) (Figure 10).

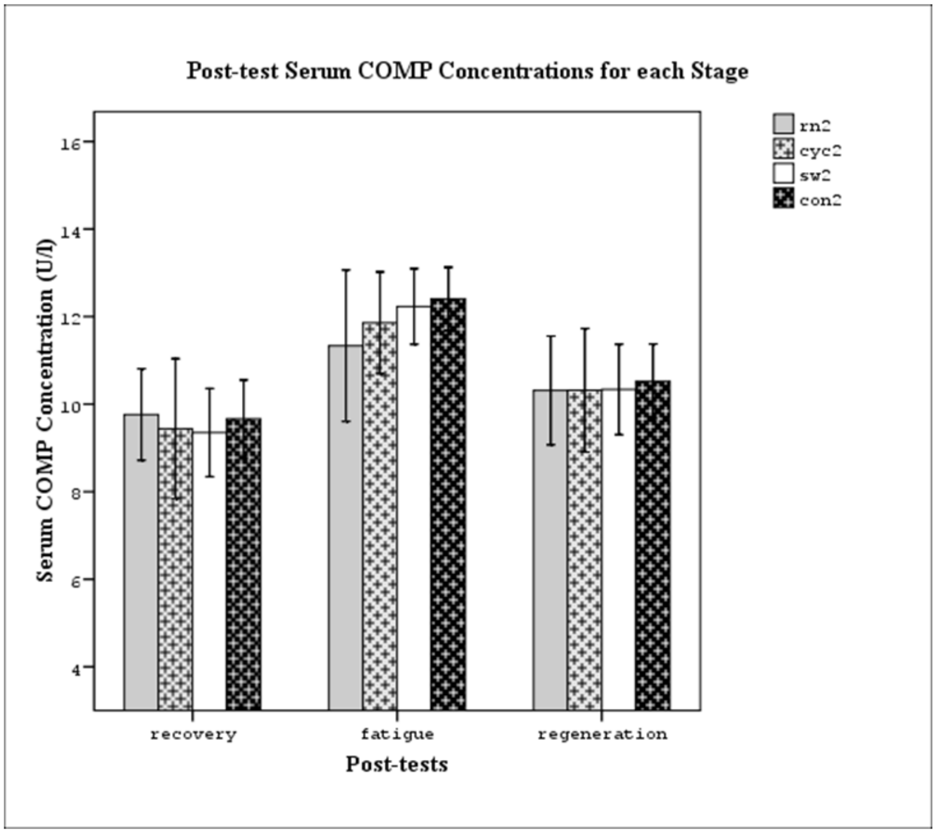


Figure 10. Serum COMP concentrations at different states during post-test measurements.

4.2.2 Serum COMP level changes due to acute exercise at pre- and post-test measurements (Deformational Behavior of Cartilage)

Multivariate tests indicate a significant fatigue or resting effect on serum COMP concentration in all experimental and control groups. Therefore, pair wise comparisons were conducted in order to assess the mean differences. Differences are tabulated in Figures 11 and 12.

Results indicated that 30 minutes of walking exercise significantly increased the serum COMP concentration in the running group at pre-tests. Also, after fatigue, 30 minutes regeneration decreased serum COMP concentration significantly in this group. However, in the post-tests measurements differences after fatigue or regeneration were not significant in the running group. Pair wise comparisons are presented in Table 7.

Table 7. Mean differences of serum COMP concentration between pairs of different states in running group.

	Running	**Mean Diff.**	**Std. Err.**	**Sig.[a]**
Pre-Test	Recovery-Fatigue	-2.87*	.85	.02
	Recovery-Regeneration	-.64	.36	.32
	Fatigue- Regeneration	2.23*	.02	.02
Post-Test	Recovery-Fatigue	-1.57	.67	.12
	Recovery-Regeneration	-.55	.29	.27
	Fatigue- Regeneration	1.02	.42	.11

Based on estimated marginal means

*. The mean difference is significant at the .05 level

a. Adjustment for multiple comparisons: Bonferroni

In the cycling group, results indicated that 30 minutes of walking exercise significantly increased the serum COMP concentration at pre-tests. Also, after fatigue, 30 minutes regeneration decreased serum COMP concentration significantly in the cycling group. In this group, 12 weeks low-impact cycling exercise did not change the adaptation capacity of the cartilage. Similar to pre-test analysis, serum COMP concentration at fatigue and regeneration increased and decreased respectively during post-tests measurements. Pair wise comparisons are presented in Table 8.

Table 8. Mean differences of serum COMP concentration between pairs of different states in cycling group.

	Cycling	Mean Diff.	Std. Err.	Sig. [a]
Pre-Test	Recovery-Fatigue	-2.66*	.46	.00
	Recovery-Regeneration	-1.27*	.38	.02
	Fatigue- Regeneration	1.39*	.18	.00
Post-Test	Recovery-Fatigue	-2.42*	.36	.00
	Recovery-Regeneration	-.88*	.26	.02
	Fatigue- Regeneration	1.54*	.24	.00

Based on estimated marginal means

*. The mean difference is significant at the .05 level

a. Adjustment for multiple comparisons: Bonferroni

In the swimming group, results indicated that 30 minutes of walking exercise significantly increased the serum COMP concentration at pre-tests. Also, after fatigue, 30 minutes regeneration decreased serum COMP concentration significantly in the swimming group. In this group, 12 weeks of non-impact swimming exercise did not change the adaptation capacity of the cartilage. Similar to pre-test analysis, serum COMP concentration at fatigue and regeneration increased and decreased respectively during post-tests measurements. Pair wise comparisons are presented in Table 9.

Table 9. Mean differences of serum COMP concentration between pairs of different states in swimming group

	Swimming	Mean Diff.	Std. Err.	Sig. [a]
Pre-Test	Recovery-Fatigue	-2.74*	.48	.00
	Recovery-Regeneration	-1.31*	.31	.01
	Fatigue- Regeneration	1.43*	.38	.01
Post-Test	Recovery-Fatigue	-2.88*	.39	.00
	Recovery-Regeneration	-.99*	.33	.04
	Fatigue- Regeneration	1.90*	.28	.00

Based on estimated marginal means

*. The mean difference is significant at the .05 level

a. Adjustment for multiple comparisons: Bonferroni

Results indicated that 30 minutes of walking exercise significantly increased the serum COMP concentration of the control participants at pre-tests measurements. Also, after fatigue, 30 minutes regeneration decreased serum COMP concentration significantly. Response of the articular cartilage to 30 minutes walking exercise stayed constant during the 12 weeks period. Pair wise comparisons are presented in Table 10.

Table 10. Mean differences of serum COMP concentration between pairs of different states in control group

	Control	Mean Diff.	Std. Err.	Sig. [a]
Pre-Test	Recovery-Fatigue	-3.03*	.42	.00
	Recovery-Regeneration	-1.05*	.28	.01
	Fatigue- Regeneration	1.98*	36	.00
Post-Test	Recovery-Fatigue	-2.74*	.32	.00
	Recovery-Regeneration	-.86*	.23	.01
	Fatigue- Regeneration	1.89*	.30	.00

Based on estimated marginal means

*. The mean difference is significant at the .05 level

a. Adjustment for multiple comparisons: Bonferroni

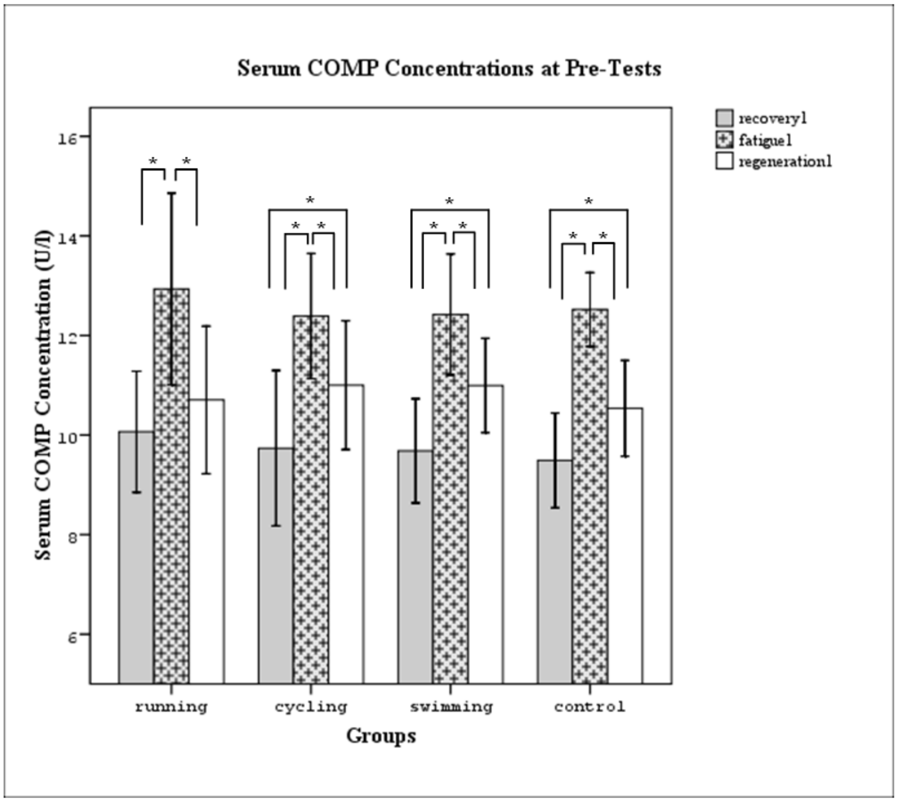


Figure 11. Pair-wise comparisons for different states for each group at pre-test measurements

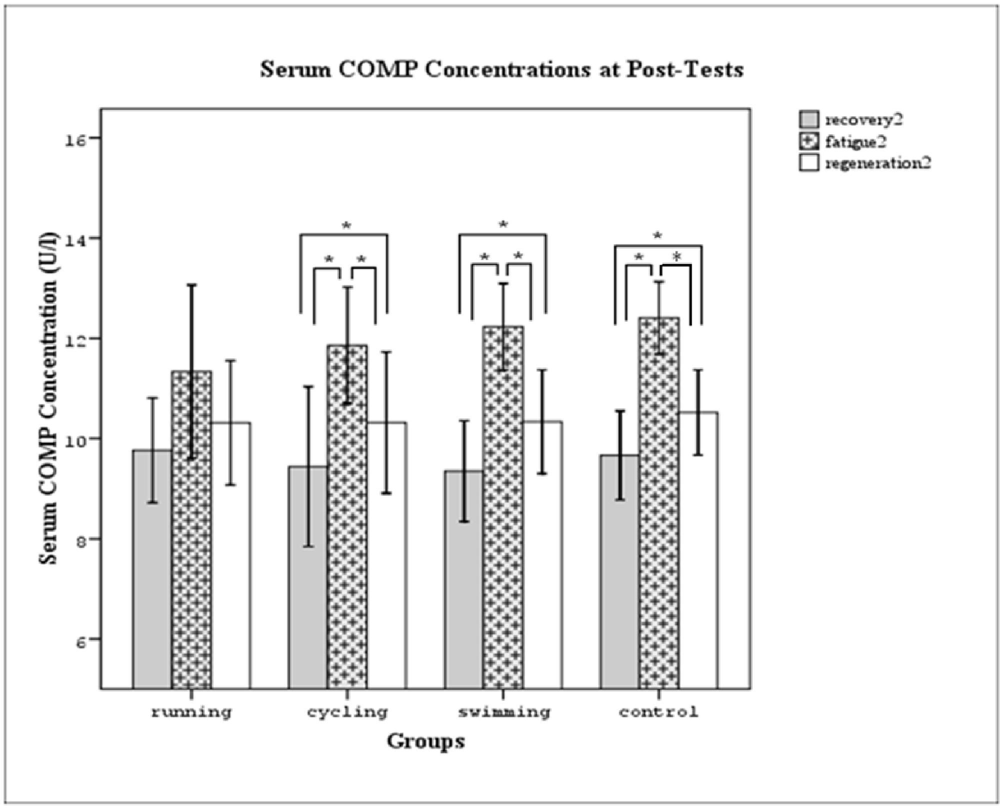


Figure 12. Pair-wise comparisons for different states for each group at post-test measurements

4.2.3 Serum COMP level changes within groups at pre- and post-test measurements

Changes of serum COMP concentrations between pre- and post-tests measurements were also evaluated. According to multivariate tests, serum COMP concentration during recovery did not decrease significantly in any of the groups (Figure 13). Statistical computations showed that in the recovery state, serum COMP concentration showed no significant main effect for Group (F (1,40) = .13, $p > .05$, $\eta^2 = .01$), Time by Group interactions (F (3,40) = 57, $p > .05$, $\eta^2 = .04$) and Time variable (F (1,40) = 1.39, $p > .05$, $\eta^2 = .03$) (Table 11).

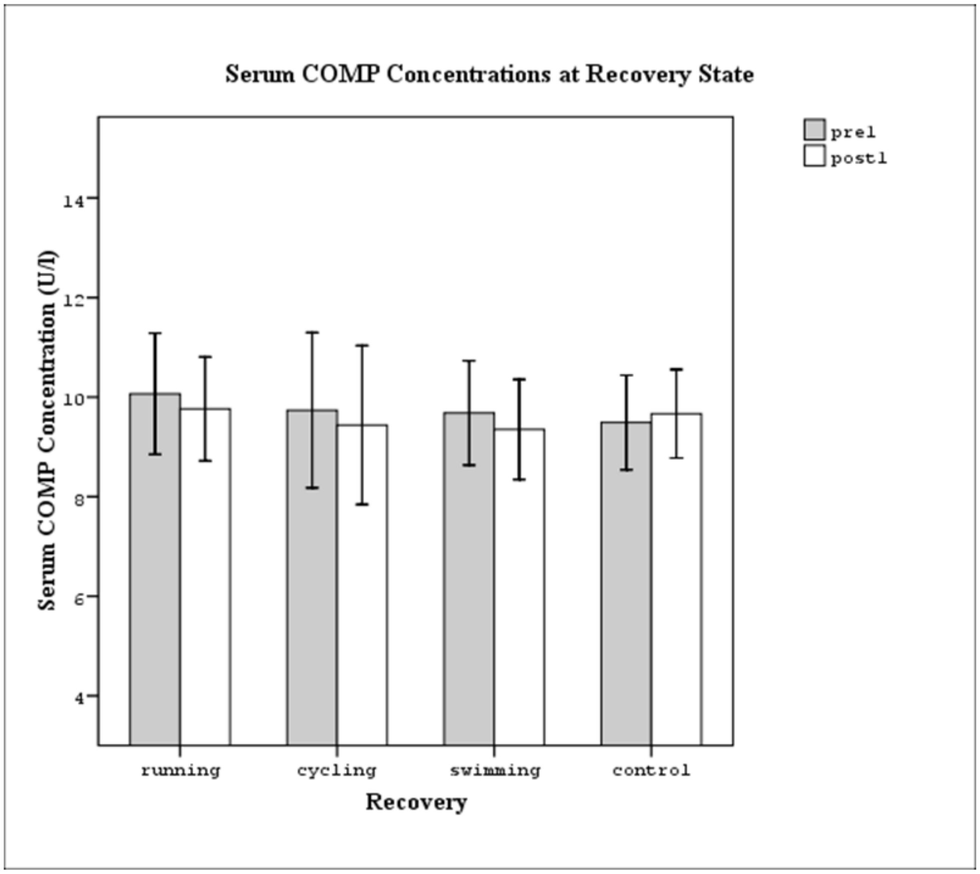


Figure 13. Pre- and post-test serum COMP level changes for each group

Table 11. Simple Effect Analysis of Time for Serum COMP Level at Recovery

Groups	**DF**	**F**	**p**
Running	1	.89	.35
Cycling	1	.85	.36
Swimming	1	1.06	.31
Control	1	.29	.59

Statistical analysis for fatigue condition showed that serum COMP concentration of the participants decreased significantly only in the running group with time. (Figure 14). Multivariate test details are as follows; Serum

COMP concentration measurement results in fatigue states showed no significant main effect for Group (F (1,40) = .09, p > .05, η^2= .01). Meanwhile, significant Time by Group interactions (F (3,40) = 4.97, p < .05, η^2= .27) and significant main effect for Time (F (1,40) = 15.74, p < .05, η^2= .28) was obtained (Table 12).

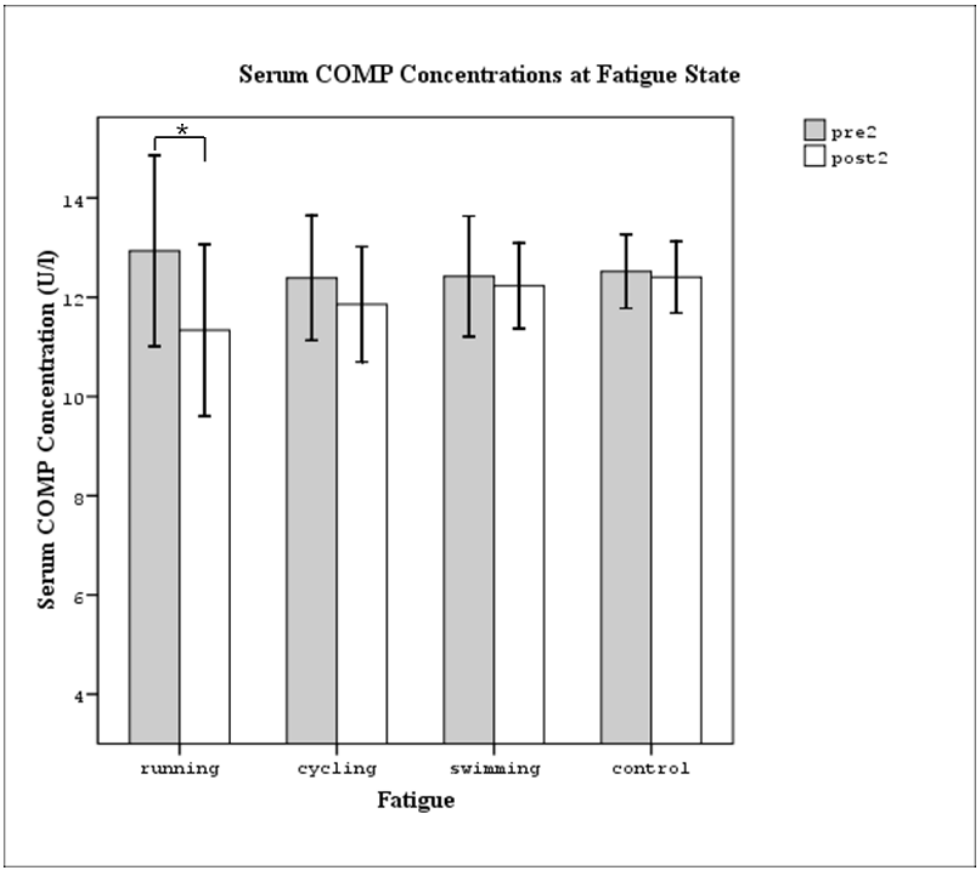


Figure 14. Pre- and post-test serum COMP level changes for each group.

Table 12. Simple Effect Analysis of Time for Serum COMP Level at Fatigue

Groups	**DF**	**F**	**p**
Running	1	27.2	.00
Cycling	1	3.0	.09
Swimming	1	.4	.54
Control	1	.1	.71

During the regeneration states of pre- and post-tests, serum COMP concentrations of the participants decreased significantly in the cycling and the swimming groups (Figure 15). Results in the regeneration states showed no significant main effect for Group ($F(1,40) = .03$, $p > .05$, $\eta^2 = .00$), or time by group interactions ($F(3,40) = .96$, $p > .05$, $\eta^2 = .07$). Meanwhile, significant main effect for Time was obtained, $F(1,40) = 7.57$, $p < .05$, ($\eta^2 = .16$) (Table 13).

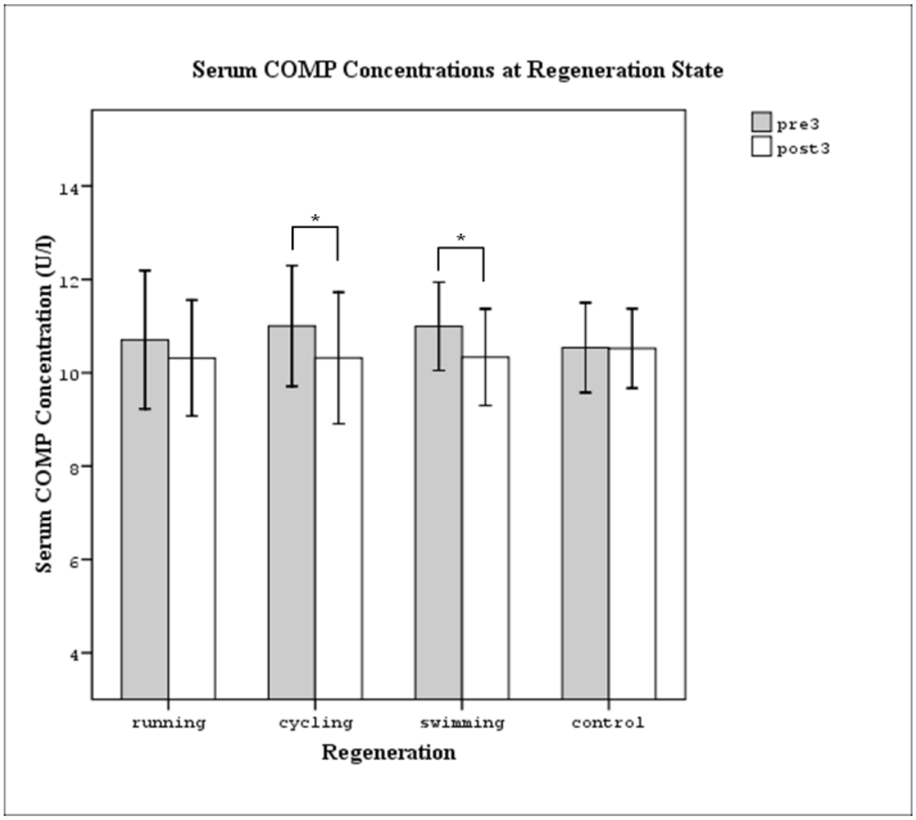


Figure 15. Pre- and post-test serum COMP level changes for each group.

Table 13. Simple Effect Analysis of Time for Serum COMP Level at Regeneration

Groups	**DF**	**F**	**p**
Running	1	1.5	.23
Cycling	1	4.6	.04
Swimming	1	4.3	.05
Control	1	.0	.96

4.3 Serum CTX-I Concentration Measurements

Pre- and post-test serum samples were analyzed for the assessment of serum CTX-I concentration changes at recovery, fatigue and regeneration phases. Descriptive statistics of serum CTX-I concentrations are presented in Tables 14 and 15.

Table 14. Pre-test Serum CTX-I concentrations (ng/mL)

	Recovery (M±SD)	**Fatigue** (M±SD)	**Regeneration** (M±SD)
Running (N=11)	.45±.07	.49±.09	.45±.08
Cycling (N=11)	.48±.10	.51±.12	.49±.10
Swimming (N=11)	.43±.12	.46±.12	.41±.09
Control (N=11)	.44±.07	.45±.06	.42±.09

Table 15. Post-test Serum CTX-I concentrations (ng/mL)

	Recovery (M±SD)	**Fatigue** (M±SD)	**Regeneration** (M±SD)
Running (N=11)	.46±.10	.48±.11	.46±.15
Cycling (N=11)	.50±.14	.51±.21	.47±.13
Swimming (N=11)	.43±.09	.46±.12	.40±.12
Control (N=11)	.42±.07	.48±.07	.44±.07

4.3.1 Serum CTX-I level differences among groups at pre- and post-test measurements

During pre-test measurements, serum CTX-I concentration analysis showed no significant differences among groups at the recovery state. Also, there were no significant differences among groups after 30 minute walking exercise. The same consistency was also valid at the regeneration measurements. Main effect for group variable at recovery state (F (3,40) = .67, Sig. of F = .58), at fatigue state (F (3,40) = .59, Sig. of F = .51) or at regeneration state (F (3,40) = 1.89, Sig. of F = .15) are presented in Figure 16.

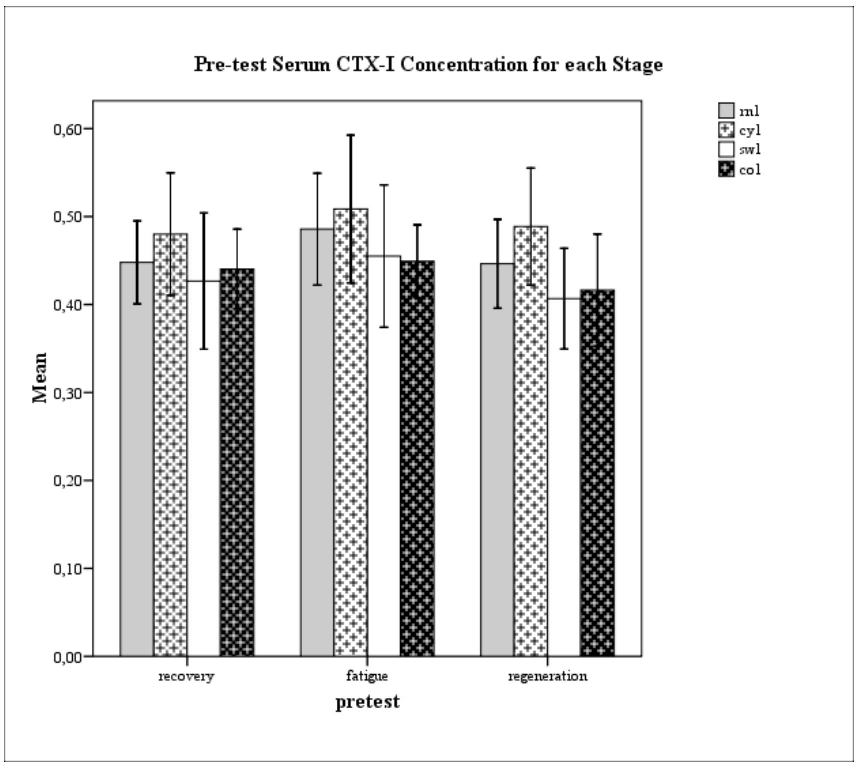


Figure 16. Serum CTX-I concentrations at different states during pre-test measurements

Serum CTX-I concentrations at the recovery state, 30 minute walking exercise and after 30 minutes regeneration, were also not significantly different among groups. Serum CTX-I concentration results showed no significant main effect for the group variable during post-test measurements at the recovery state (F (3,40) = 1.24, Sig. of F = .31), at the fatigue state (F (3,40) = .28, Sig. of F = .84) or at the regeneration state (F (3,40) = .70, Sig. of F = .56) (Figure 17).

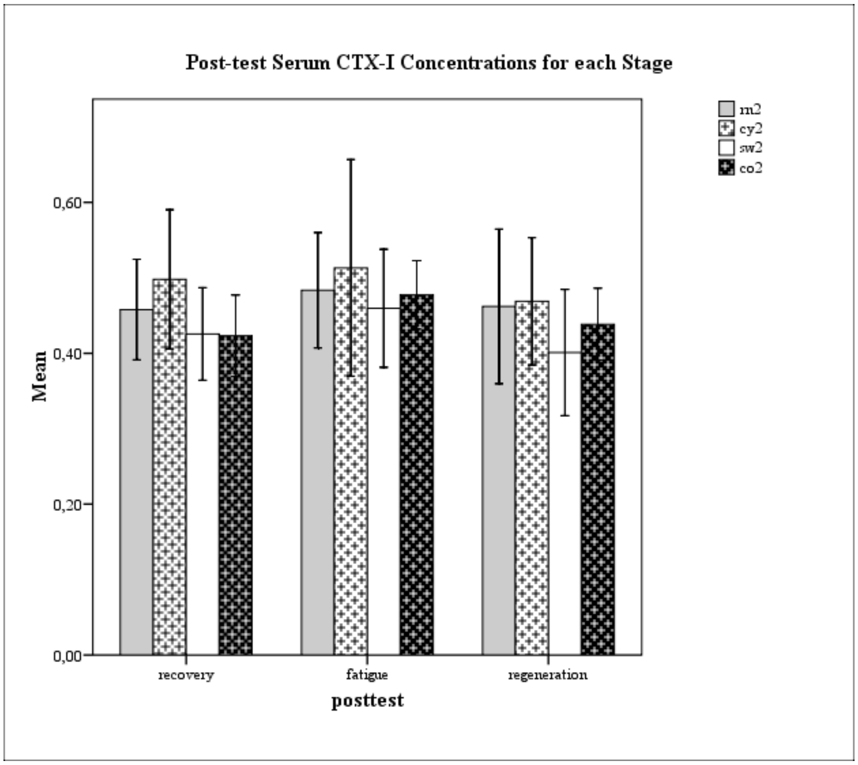


Figure 17. Serum CTX-I concentrations at different states during post-test measurements

4.3.2 *Serum CTX-I level changes due to acute exercise at pre- and post-test measurements*

Multivariate tests indicate that fatigue or resting effect was not significant on serum CTX-I concentration in all experimental and control groups. Nevertheless, pair wise comparisons were conducted in order to assess the level of statistical differences. Results indicated that a significant difference among the different states of measurements was not observed in any of the groups.

Results indicated that 30 minutes of walking exercise did not affect the serum CTX-I concentration in the running group significantly at pre-tests. Also, after 30 minutes regeneration, serum CTX-I concentration did not change significantly in this group. Similar results were observed at post tests.

Differences after fatigue or regeneration were not significant in the running group. Pair wise comparisons are presented in Table 16.

Table 16. Mean differences of serum CTX-I concentration between pairs of different states in running group.

	Running	Mean Diff.	Std. Err.	Sig.[a]
Pre-Test	Recovery-Fatigue	-.04	.02	.37
	Recovery-Regeneration	.00	.01	1.00
	Fatigue- Regeneration	.04	.02	.07
Post-Test	Recovery-Fatigue	-.03	.02	.52
	Recovery-Regeneration	-.00	.03	1.00
	Fatigue- Regeneration	.02	.03	1.00

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni

Also in the cycling group, results indicated that there were no significant differences among recovery, fatigue or regeneration states in the pre and the post tests. Pair wise comparisons are presented in Table 17.

Table 17. Mean differences of serum CTX-I concentration between pairs of different states in cycling group.

	Cycling	Mean Diff.	Std. Err.	Sig.
Pre-Test	Recovery-Fatigue	-.03	.01	.07
	Recovery-Regeneration	-.01	.01	1.00
	Fatigue- Regeneration	.02	.02	.77
Post-Test	Recovery-Fatigue	-.02	.03	1.00
	Recovery-Regeneration	.03	.02	.77
	Fatigue- Regeneration	.04	.04	.96

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni

In swimming group, 30 minutes walking exercise did not cause any accumulation of serum CTX-I level at pre or post tests. Similarly, 30 minutes regeneration did not trigger elimination of serum CTX-I level. Pair wise comparisons are shown at Table 18.

Table 18. Mean differences of serum CTX-I concentration between pairs of different states in swimming group.

	Swimming	**Mean Diff.**	**Std. Err.**	**Sig.**
Pre-Test	Recovery-Fatigue	-.03	.03.	.98
	Recovery-Regeneration	.02	.02	.82
	Fatigue- Regeneration	.05	.03	.39
Post-Test	Recovery-Fatigue	-.03	.02	.17
	Recovery-Regeneration	.03	.03	1.00
	Fatigue- Regeneration	.06	.03	.14

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni

Serum CTX-I concentration in control group was not changed like all other groups in any states during pre or post tests. Pair-wise comparisons are shown at Table 19.

Table 19. Mean differences of serum CTX-I concentration between pairs of different states in control group.

	Control	Mean Diff.	Std. Err.	Sig.
Pre-Test	Recovery-Fatigue	-.01	.00	.19
	Recovery-Regeneration	.02	.03	1.00
	Fatigue- Regeneration	.03	.03	.84
Post-Test	Recovery-Fatigue	-.05	.02	.11
	Recovery-Regeneration	-.02	.01	.57
	Fatigue- Regeneration	.04	.01	.062

Based on estimated marginal means

a. Adjustment for multiple comparisons: Bonferroni

4.3.3 *Serum CTX-I level changes within groups at pre- and post-test measurements*

Changes of serum CTX-I concentrations between pre- and post-tests measurements were also evaluated. According to multivariate tests, serum CTX-I concentration during recovery did not decrease significantly in any of the groups (Figure 18). Statistical computations showed that in the recovery state serum CTX-I concentration showed no significant main effect for Group ($F (1,40) = 1.22$, $p > .05$, $\eta^2 = .84$), Time by Group interactions ($F (3,40) = .27$, $p > .05$, $\eta^2 = .02$) and Time variable ($F (1,40) = .03$, $p > .05$, $\eta^2 = .00$) (Table 20).

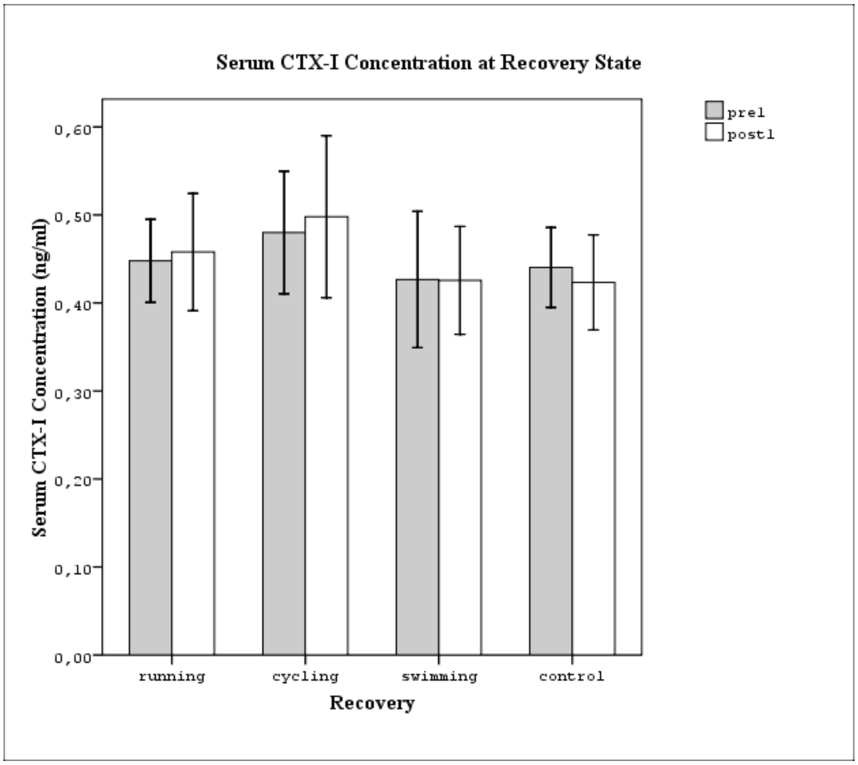


Figure 18. Pre- and post-test serum CTX-I level changes for each group

Table 20. Simple Effect Analysis of Time for Serum CTX-I Level at Recovery

Groups	DF	F	p
Running	1	.12	.73
Cycling	1	.38	.54
Swimming	1	.00	.97
Control	1	.34	.56

Statistical analysis for the fatigue condition showed that serum CTX-I concentration of the participants did not decrease significantly in any of the groups (Figure 19). Serum CTX-I concentration measurement in the fatigue state showed no significant main effect for Group ($F (1,40) = .63$, $p > .05$, $\eta^2 = .05$), Time by Group interactions ($F (3,40) = .11$, $p > .05$, $\eta^2 = .01$) and Time variable ($F (1,40) = .18$, $p > .05$, $\eta^2 = .01$) (Table 21).

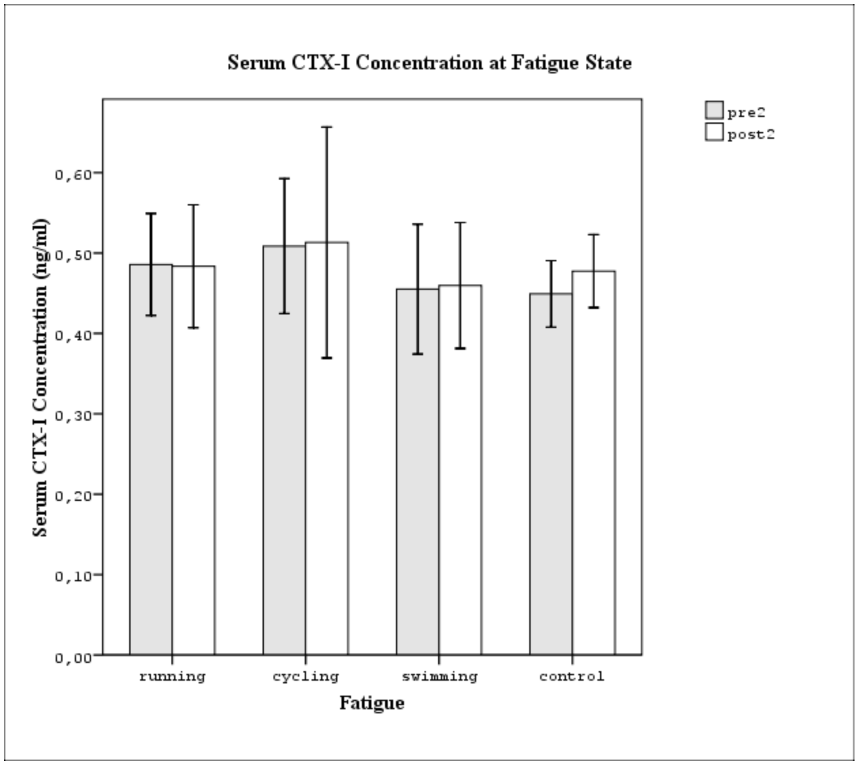


Figure 19. Pre- and post-test serum CTX-I level changes for each group

Table 21. Simple Effect Analysis of Time for Serum CTX-I Level at Fatigue

Groups	DF	F	p
Running	1	.00	.96
Cycling	1	.01	.91
Swimming	1	.01	.91
Control	1	.47	.50

During regeneration states of pre- and post-tests, serum CTX-I concentrations of the participants did not change significantly in any of the groups (Figure 20). Detailed statistics showed that serum CTX-I concentration measurement results in the regeneration states showed no significant main effect for Group ($F(1,40) = 1.43$, $p > .05$, $\eta^2 = .10$), Time by Group interactions ($F(3,40) = .31$, $p > .05$, $\eta^2 = .02$) and Time variable ($F(1,40) = .03$, $p > .05$, $\eta^2 = .00$) (Table 22).

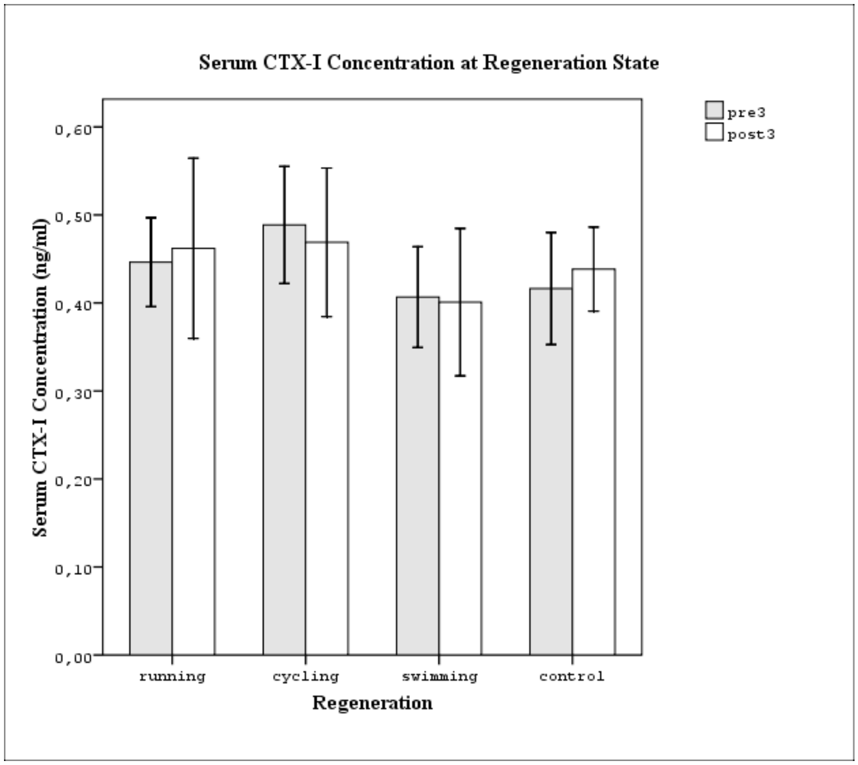


Figure 20. Pre- and post-test serum CTX-I level changes for each group

Table 22. Simple Effect Analysis of Time for Serum CTX-I Level at Regeneration

Groups	DF	F	p
Running	1	.21	.65
Cycling	1	.33	.57
Swimming	1	.03	.87
Control	1	.41	.53

CHAPTER 5

DISCUSSION

The purpose of this study was to compare changes of deformational behavior and functional adaptation of articular cartilage and bone after 12 weeks moderate amount of high-impact, impact or non-impact physical exercise program by measuring biochemical markers of cartilage and bone degradation.

This chapter discusses effects of different exercise interventions on some biomotor abilities and short term (deformational behavior) or long term (functional adaptation) changes of knee articular cartilage and bone. After an extensive literature review, two main hypotheses and six sub-hypotheses were constructed. In the light of our findings, these hypotheses are discussed in this chapter.

Participants of this study were 44 healthy male university students. Inclusion criteria were no previous history of lower extremity surgery and refrainment of regular sports activity.

Participants trained for 12 weeks according to the ACSM's guidelines for endurance development. All three activities were continuous cyclic exercises but impact levels were changing from low to high.

The results of the present study showed that all endurance exercises significantly changed body composition and endurance capacities of participants but changes in isokinetic strength capacity increased significantly only in the swimming group. Biochemical marker of cartilage degeneration (COMP) measurements showed that 30 minutes walking exercise did not significantly increase the level of cartilage degeneration after 12 weeks of high impact running exercise. However, level of CTX-I was not affected by 30 minutes of exercise neither in pre-post tests, nor in any groups.

5.1 Physical and Biomotor abilities of participants

General implication of all kinds of endurance exercises is decreasing body mass index (BMI) and increasing maximum oxygen consumption (VO_2max). In the present study, groups performed three different endurance type activities for 12-weeks. Forms of activities were different but most importantly quantitative elements of the exercises were similar. Volume of exercises were 40 minutes per session, densities were three days a week for 12 weeks and intensity of exercises were 60-70 % of heart rate reserves. This amount of exercise caused a significant decrease in BMI and a significant increase in VO_2max in all experimental groups. However, isokinetic strength significant increased only in the swimming group.

Changes in BMI and VO_2max can partially be explained by functional adaptation (Darwin., 1872). Hippocrates, also claimed that all parts of the body that have a function, if used in moderation and exercised in labour in which each is well developed and age more slowly (Hippocrates, as cited in Paffenbarger, 2001). Therefore improvement in maximal oxygen consumption and decrease in fatness were expectable results. In a similar study design, Scharhag-Rosenberger et al. (2009) observed a significant decrease in the body weights of healthy untrained subjects after six months of moderate intensity jogging/walking exercises. Additionally, significant increase in VO_2max occurred at third months of intervention and continued along the 12 months intervention. However, Scharhag-Rosenberger and collaborates did not use a control group in their study. In our study, we applied three different exercise interventions in three groups and additionally a control group participated in the tests but did not attend in any physical exercise during the 12 weeks of assessment. VO_2max improved in all groups but this change was significant only in the exercise groups. Changes of VO_2max among experimental groups were not significantly different in our study. Lieber, Lieber, & Adams (1989) investigated the effects of run-training and swim-training at similar absolute intensities on treadmill VO_2max. In their randomized control trial, they observed that runners, swimmers, and controls experienced a significant increase in treadmill VO_2max over the 11 1/2-week study period. However, 28% and 25% increases in VO_2max observed for the runners and swimmers, respectively; these were significantly greater than the 5% increase observed for the controls.

In this study different types of exercises were performed for 12 weeks. Common trait of these exercises was cyclic-endurance type of exercises. Therefore, improvement of isokinetic strength was not a certain prospect for our study. However, isokinetic strength increased significantly in the swimming group. This change may be explained by the nature of aquatic resistance. Isokinetic contraction can be produced by special designed machines but according to Fox, Bowers, & Foss (1988) arm stroke during freestyle swimming is a good example of natural isokinetic contraction. Moreover, some researchers attempted to establish reliable swimming simulators which were isokinetic dry-land swim benches or they used isokinetic swim benches as reliable representative of water resistance (Swaine, 1997; Konstantaki, Trowbridge, & Swaine 1998). Our findings are also parallel with the findings of Gehlsen, Grigsby, & Winant (1984). Although swimming is an endurance type of sport, Gehlsen and collaborates observed that aquatic fitness programs increased isokinetic peak torque values of knee extensor and flexor muscles.

5.2 Serum COMP levels

Differences between serum COMP levels of different groups at each state were not statistically significant in pre-test measurements. Similarly, there were no significant differences in serum COMP concentrations between the groups at each state during post-test. Thirty minutes moderate walking exercise increased serum COMP concentration in participants at pre-test measurements. After thirty minutes walking, participants rested on o chair for thirty minutes. This regeneration period caused a significant decrease of serum COMP concentrations.

This kind of serum COMP responses to acute exercise was also observed by Mundermann and her collaborates (2005). In their study, serum COMP levels of ten adults increased significantly after 30-min outdoor walking at their self-selected normal speed. Mundermann's study was the first attempt to link serum COMP concentration to physiological cyclic loading in vivo. Similar findings were observed by Andersson et al. 2006. They observed that serum COMP levels increased during exercise in individuals with knee osteoarthritis, whereas levels decreased during rest.

Kersting et al. (2005) also investigated the relationship between the effect of running on cartilage volume and serum COMP concentration. Similar to our findings, resting COMP level was lower than fatigue serum COMP level.

However, this elevation was not significant in their study. This contradictory finding of the study might be related to the time of blood sampling. In their study, Kersting and collaborates collected post-exercise blood samples 25 min after training which was immediately after the post-activity MRI. In spite of this delayed sampling, general findings of their study were parallel with the findings of the present study. Multiple regression analysis showed that resting COMP and COMP changes after 1 h running explained the variance of cartilage volume changes.

Acute effect of physical exercise on articular cartilage was also evaluated by MRI studies. Findings of MRI studies were generally parallel to our biochemical measurements. Significant amount of deformational behavior after exercise was observed morphologically in these studies. Eckstein and collaborates (1998) mentioned a deformational behavior of articular cartilage after repetitive knee bending exercise. After several sets of knee bending exercises, a statistically significant decrease in cartilage volume was observed. In a subsequent study, Eckstein et al (1999) observed a deformation of articular cartilage after 50 knee bending ranged from 2.4 to 8.6 %. More repetition or repeated sets of exercise with intervals did not cause further deformation. Eckstein and his colleagues (2000) also compared the effect of dynamic versus static loading on deformational behavior of articular cartilage. In this study, researchers observed a significant reduction of articular cartilage volume after dynamic or static loading. However, the volume changes were significantly lower after static loading than after dynamic loading. The maximal thickness of cartilage also decreased significantly due to both types of loading.

Eckstein et al., (2005) evaluated the effect of different types of activity. They compared effect of knee bends, squatting, normal gait, running and cycling.

Finding of this study demonstrated that knee bending as high impact loading caused highest deformation and normal gait caused lowest deformation on patellar cartilage deformation. This result mentioned that articular cartilage deformation is directly dose dependent response. In contrast to Eckstein and collaborates, in a very recent study, Niehoff et al., (2008) observed that 30 min running exercise enhanced the serum COMP concentration but slow knee bends did not cause any significant change.

Articular cartilage contributes to transferring enormous loads as uniformly as possible from one skeletal segment to the next. According to Kessler et al., (2006) whether it manages this task when subjected to the high repetitive loading cycles occurring during long-distance running and can remain intact is still the topic of controversy. Therefore, in recent years, possible deleterious effects of competitive exercises, especially long distance running, have been the subject of interest (Hofmann,Wortler & Imhoff, 2004; Kim, Lee & Kim, 2007; Kessler et al., 2008; Kim, Lee & Kim, 2009). Hofmann et al investigated whether external impact loading in marathon running creates an internal stress on bone and cartilage that are demonstrable on MRI. MR images did not demonstrate any deleterious signs after post marathon run. Hofmann suggested that high impact forces, created by long distance running, are well tolerated and changes are not detected by MR images, whereas our results showed that there is a significant degradation of articular cartilage according to elevation of biochemical markers at serum after lower extremity exercise. In another long-distance running study Kessler et al., (2008) refute the assertion of Hofmann. They found a significant reduction after running even moderate distances and also 60 minutes recovery was sufficient for significant regeneration of cartilage volume.

MRI studies shows that competitive long distance running decreases the volume and thickness of articular cartilage at knee region morphologically. From another perspective, Kim, Lee & Kim (2007) evaluated the biomarkers of muscle and cartilage damage during a 200 km run. They measured the serum COMP content before, midway and immediately after the race. Serum COMP level increased 1.3-fold at 100 km and 3-fold at the finish of the 200 km running race. This result mentioned that ultra-marathon running event may be detrimental for articular cartilage and may increase the incidence of degenerative conditions in later life. Kim, Lee & Kim (2009) also compared the cartilage damage between different long distance running competitions. They also evaluated serum COMP level changes after recovery periods. Similar increase was observed after marathon run like ultra-marathon. However, serum COMP level declined to the pre-race level after 2 days recovery after marathon race. Researchers observed that serum COMP only returned to the pre-race level on day 6. This amount of impact exercise may have detrimental effect on cartilage and the time for recovery may extend for many days.

It seems that the physical activity causes a deformational effect on articular cartilage. Our finding about deformational behavior of articular cartilage was parallel with the findings of other studies. The literature presents that extremely long duration of exercise causes more serious deformation in joint cartilage and a longer recovery period is needed for regeneration. However, intensity of our walking test during blood sampling is relatively lower and duration of protocol was shorter. Our results and literature support the idea that 30 minutes of exercise is enough to observe a significant deformation in articular cartilage and 30 minutes of resting is an adequate period for recovery. In addition to the effect of exercise on articular cartilage, literature supports our finding about the high sensitivity of the COMP measurement technique as a consistent biomarker for cartilage degeneration.

In our study, after pre-test measurements, participants were divided into four groups randomly. Each group accomplished their groups exercise requirements for a 12 weeks intervention period. After interventions, post-test measurements were performed and similar serum COMP responses were observed. During post-test measurements, thirty minutes walking exercise increased serum COMP levels of the cycling and the swimming groups significantly. However, this increase was not significant in the running group. Also, the serum COMP concentration at fatigue state was significantly lower in the post-test measurement than that of the pre-test measurement in the running group. However, pre- and post-test serum COMP concentration difference, after thirty minutes of walking exercise, were not significant neither in the cycling nor in the running groups.

Although it is obvious that immobilization has a deterioration effect on cartilage, there is no consensus on the functional adaptation ability of articular cartilage for fitness exercise in the literature. It is known that unloading during long space flight decreases the BMD and increases the bone fracture risks (Lang, 2006; LeBlanc, Spector, Evans & Sibonga, 2007). Articular cartilage also has mechanical functions like the bone tissue. Vanwanseele, Lucchinetti & Stussi (2002) mentioned a 9% decrease in articular cartilage thickness after 11 weeks of immobilization. Also Vanwanseele, Eckstein, Knecht, Stussi, & Spaepen, (2002) evaluated the tinning of knee cartilage. Their data showed that progressive atrophy of human cartilage occurs in spinal cord-injured patients because of absence of normal joint loading. Six years ago, Vanwanseele, Eckstein, Knecht, Spaepen, & Stussi (2003) firstly reported a longitudinal analysis of cartilage atrophy in patients with spinal cord-injured. They reported that human cartilage atrophies during unloading is higher than that observed in osteoarthritis patients.

In these spinal cord-injury studies, not only skeletal unloading induced defect was occurred, but also restricted joint motion was another possible treat for cartilage defect. In a very recent study, Tomiya et al., (2009) investigated the effect of long-term skeletal unloading without restriction of joint motion on the patella. They observed that a full-thickness cartilage defect was revealed in 88.6% of tail suspended rats. Their finding shows that impact or loading is another important component of healthy cartilage. In our study, subjects were active and they were subjected to some different amount of impact load on articular cartilage in addition to daily life. Parallel with the findings of the Tomiya, we observed a better adaptation in high-impact running group.

In addition to unloading and cartilage relationship, effects of overloading and sport-exercise on articular cartilage of animals and human with patients, healthy subjects and athletes were also evaluated.

In preliminary studies, researchers found positive effect of exercise on articular cartilage on animal studies. Kiviranta, Tammi, Jurvelin, Saamanen, & Helminen, (1988) measured the local influences of physical exercise on thickness of canine articular cartilage. Findings of their study demonstrated that moderate running exercise locally alters the biological properties of young articular cartilage at regions of bearing the highest loading surplus. Also, in 1993, Lammi and collaborates examined the effects of long-term long-distance running on the metabolism of articular cartilage of young beagles. Post-test measurements at their study showed that the articular cartilage of the femoral head showed a great capacity to adapt to the increased mechanical loading.

According to Hunter & Eckstein (2009), exercise has positive salutary benefits for joint tissue in addition to its other health benefits. Also, therapeutic exercise is an invaluable component to a comprehensive treatment program for patients with osteoarthritis (Stitik, Gazzillo, & Foye 2007). Therefore, effects of exercise in some arthritis patients were also evaluated. Lin, Davey, & Cochrane, (2004) examined the effectiveness of a community-based water exercise program on measures of self-reported health and physical function with knee-hip osteoarthritis. Results showed that older people with knee/hip OA gained modest improvements in measures of physical function, pain, general mobility and flexibility after participating in 12 months of community-based water exercise. In addition to improvements in physical function due to physical exercise, Ross & Dahlberg (2005) also indicated that adult human articular cartilage has a potential to adapt to loading change. Moderate exercise may be a good treatment not only to improve joint symptoms and function, but also to improve the knee cartilage glycosaminoglycan content, an important aspect of the biomechanical properties of cartilage, in patients at high risk of developing OA.

In addition to previous sports related studies, Wijayarante et al., (2008) investigated the determinants of change in patellar cartilage volume among healthy middle-aged women. In this study self-reported exercise was assessed by questionnaire. Researchers observed that annual loss of patella cartilage volume was 1.6% and age was positively associated with patella cartilage volume loss. They also found that fortnightly participation in exercise promoting an increased heart and respiratory rate for at least 20 min also tended to be associated with a reduced rate of patella cartilage volume loss. Results of their study revealed that exercise participation tends to be associated with a reduction in the rate of patella cartilage volume loss. Similarly, Koo &

Andriacchi (2007) claimed that individual variations in cartilage thickness can be associated with both individual variations in joint loading associated with activities of daily living as well as individual differences in the anatomy of the contacting surfaces of the joint. They suggested that the dynamics of walking is an important factor to describe individual differences in cartilage thickness for normal subjects.

Morphologic characteristics of knee cartilage of elite athletes and inactive subjects were compared in some studies (Muhlbauer et al., 2000; Eckstein et al., 2002; Eckstein et al., 2006; Eckstein, Hudelmaier, & Putz 2006; Gratzke et al., 2007). MRI results of Muhlbauer showed that mean or maximal thickness of knee cartilage was not significantly different in triathletes when compared with inactive volunteers. Also, Eckstein et al., (2002) could not find a significant difference between the knee joint cartilage thickness of triathletes and inactive volunteers. This finding is unexpected in the view of the functional adaptation observed in other musculoskeletal tissues and seems like controversial with our results. However, results of Gratzke et al., (2007) explain this controversial condition somehow. In their study, weight lifters and sprinters displayed significantly greater cartilage thickness only in patella than nonathletic volunteers but findings suggested that cartilage thickness has much less ability to adapt to mechanical loading than muscle. However, as mentioned in a review of Eckstein, Hudelmaier, & Putz (2006) whereas ‘more’ muscle provides more tensile strength, and ‘more’ bone provides higher structural compressive and bending strength and hence better protection against fractures, ‘more’ cartilage is not known to be associated with improved mechanical competence of joints. Therefore, functional adaptation of articular cartilage may not be directly related with the enlargement of the cartilage morphology.

Patellar cartilage deformation after physical exercise was compared in some professional athletes and untrained volunteers by Eckstein et al (2006). In this study, researchers evaluated both the effect of exercise on deformational behavior and functional adaptation of articular cartilage. They found a significant deformation after physical exercise. However, no significant difference was found between athletes and non-athletic controls. Therefore, researchers claimed that functional adaptation of human articular cartilage is limited or not. The results of our study refute this statement. A significant functional adaptation was observed in high impact running group in our study as reported in some previous studies. Also finding of Qi & Changlin (2007) supports our results and explains the weakness of the study of Eckstein and colleagues. According to Qi & Changlin, long-time and high-intensity movement training induces cartilage degeneration in knee joint. Within the intensity extent applied in their study, knee cartilage degeneration caused by light training or intensive training has no difference in MR imaging, but has a comparatively obvious difference in biomarkers level. This finding demonstrates that several biomarkers have a very good practical value in detection of articular cartilage degeneration in early stages.

Fole et al., (2007) suggested that knee cartilage volume and tibial plateau are dynamic structures that can respond to physical stimuli. Fole also claimed that muscle strength and endurance fitness may be protective against cartilage loss. In their longitudinal study, Racunica et al., (2007) observed that vigorous physical activity appears to have a beneficial effect on knee articular cartilage in healthy adults with no history of knee injury or disease. Therefore, they concluded that a beneficial effect of physical activity for diseases associated with aging and suggests that exercise that is good for the heart is also good for the knees.

5.3 Serum CTX-I levels

Similar to serum COMP concentrations, differences between serum CTX-I concentrations of different groups at each state were insignificant in pre-test measurements. Also, there were no significant differences between the groups at each state during post-test serum CTX-I concentrations. In contrast to COMP responses, thirty minutes moderate walking exercise did not increase serum CTX-I concentration significantly in all sedentary participants at pre-test measurements. Regeneration period after fatigue caused a slight decrease of serum CTX-I concentrations in participants but this decrease was insignificant.

Post-test measurements showed that serum CTX-I responses to exercise were similar to pre-test results. Post-test results showed that slight changes after 12 weeks exercise intervention were not significant in any exercise groups or the control group.

CTX-I also is a biomarker of collagen degradation but it is specific for bone. Everts &Buttle (2008) explained that degradation of type I and II collagen results in release of C-terminal telopeptides. According to Garnero et al., (2001), CTX-I levels decreased in patients with knee OA. They suggested that knee OA appears to be characterized by a systemic decrease of bone turnover. In 2002, Garnero and his collaborates also observed that high baseline levels of urinary CTX-I and CTX-II independently predict an increased risk of radiologic progression over 4 years in patients with early RA, especially those without radiologic joint damage. Therefore, they concluded that CTX-I and CTX-II may be useful for identifying individual RA patients at high risk of progression very early in the disease, before erosions can be detected radiographically. Also in their review, Raissouni, Gossec, Ayral, & Dougados (2005) mentioned that high levels of CTX-I and CTX-II strongly predict the development of joint erosions before the occurrence of radiological joint damage.

Measurement of CTX-I changes are also accepted as a useful tool of prosecution of treatment in some arthritis. Bjarnason & Christiansen (2000) suggested that early CTX-I measurements predict long-term preservation of bone mass during hormone replacement therapy. Also, in their study, d'Elia et al (2004) evaluated the effects of hormone replacement therapy on markers of bone and cartilage metabolism in rheumatoid arthritis patients. In this study treatment with hormone replacement therapy resulted in decrease in CTX-I and COMP at 2 years. Researchers concluded that CTX-I reflected bone turnover very sensitively and they suggested that biochemical markers of bone and cartilage turnover may provide a useful tool for assessing novel treatment modalities in arthritis, concerning both joint protection and prevention of osteoporosis.

In spite of its high sensitivity in the diagnosis of the arthritis or prosecution of treatment, sensitivity of bone specific biomarkers in the sport related studies are controversial. In a preliminary study Bennell et al (1998) evaluated bone turnover in stress fractured athletes and they emphasized that single and multiple use of biomarkers are not clinically useful in predicting the likelihood of stress fractures in athletes. Also Bennell et al., (1997) evaluated bone turnover in different sports groups in a 12-month longitudinal study. Bennell et al observed that levels of bone markers were not predictive of subsequent changes in bone metabolism.

O'Kane, Hutchinson, Atley, & Eyre (2006) compared the sport-related differences in biomarkers of bone resorption and cartilage degradation in endurance athletes. As we know, only O'Kane and friends found that athletes in-training in different sports show significant differences in these markers. In our study, however, we could not find a significant difference between the levels of CTX-I in different endurance exercise groups. The main probable reason of this finding is the fact that inactive volunteers took part in our study. Moreover, this 12-week duration and fitness level exercises were not enough to stimulate the accumulation of serum CTX-I concentration. Our findings are parallel with some other researches. Creighton, Morgan, Boardley, & Brolinson (2001) evaluated markers of bone turnover in female athletes comparing three impact groups, high impact, medium impact and nonimpact, with sedentary age-matched controls. In this study no differences in a marker of bone resorption were noted. Also in a very recent study, Lester et al., (2009) sought to determine whether aerobic, resistance, or combined aerobic and resistance exercise programs conducted over eight weeks and compared to a control group could produce changes in biochemical markers of bone turnover indicative of bone formation. Similar to our findings, Lester and his colleagues did not find a significant change in the level of CTX-I. The results of their study demonstrate that during eight weeks physical training program CTX-I concentrations were similar in all four groups pre-training and remained stable throughout the training programs. This stability of CTX-I responses against the physical exercise is also related with the sensitivity of the marker. According to Whipplle et al., (2004), markers of bone degradation are disadvantageous because of the lack of sensitivity and tremendous variability between individuals. Also, Whipplle reported that there is no definite statistical data to correlate to a gold standard when used to assess markers response to exercise.

CHAPTER 6

SUMMARY, CONCLUSIONS & RECOMMENDATIONS

6.1 Summary

The objective of the present study was to investigate deformational behavior and functional adaptation of articular cartilage by the changes of serum level of Cartilage Oligomeric Matrix Protein (COMP) and C-terminal telopeptides of collagen type I (CTX-I) during a 30-min acute exercise after 12-weeks of regular high impact, impact and non-impact endurance exercise.

In this study, results showed that 12-weeks endurance exercise elicited improvements of some important health related parameters in all exercise groups. BMI of participants decreased and VO_2max increased significantly in all exercise groups.

In the analysis of serum COMP comparisons, multivariate tests indicated a significant fatigue or resting effect on serum COMP concentration in all experimental and control groups at pre- and post-tests. According to this finding post-hoc pair-wise comparisons were applied. These univariate tests indicated significant differences during post test measurements among rest, fatigue and regeneration phases in all groups except running.

On the other hand, multivariate analysis showed that fatigue or resting could not elicit a significant change of serum CTX-I concentrations in any experimental or control groups at the beginning or the end of the intervention period.

6.2 Conclusions

In this study, experimental groups achieved significant increase in endurance performance and they reached higher capacities on consumption of oxygen. Also, BMI of the experimental groups decreased significantly. These improvements are evidence of beneficial effects of regular exercise for general health.

Also, we hypothesized that all the body systems adapt their functions according to environmental stimulus; therefore, we expected a functional adaptation of weight bearing articular cartilage due to regular sports activities. At the beginning of the study, 30 minutes moderate walking activity increased serum cartilage specific OA biomarker concentration but not bone specific OA biomarker concentration of young sedentary men. 12 weeks regular high, moderate or low impact physical exercise could not change the behavior of CTX-I concentration in serum. However, weight-bearing high impact physical exercise (running) caused a decrease in the effect of moderate activities on serum COMP accumulation.

This kind of decrease in the accumulation of cartilage deformation marker after 12 weeks of regular high impact loading explains the functional adaptation ability of articular cartilage to specific environmental requirements.

According to the results of this study, regular moderate volume and intensity of endurance exercise are recommended for general health benefits. In addition to general health benefits, exercises like running or jogging, which create enough stimuli for functional adaptation, are recommended for the consolidation of articular cartilage tissue in healthy young men. Also high impact exercises can be added into the training programs of low-impact sports athletes for their future general health.

6.3 Recommendations

Up to date, literature focused on cartilage of animals, cartilage of patients and differences of athletes' cartilage from normal population. Our investigation is one of the first cause-effect studies about the responses of the healthy human articular cartilage. We also examined the responses of the articular cartilage biochemically.

In this study, we examined the effect of endurance exercise on knee articular cartilage of healthy young men. However, further studies about the effect of exercise on human articular cartilage are necessary.

Besides the articular cartilage of healthy male, deformational behavior and functional adaptation of females' articular cartilage is a valuable subject to examine because other similar tissues like muscle or bone of females have different responses to exercise than males.

Another important issue is the maturation of participants. Responses of articular cartilage for exercise during developmental ages should be examined in further studies. Response of articular cartilage at developmental ages and elderly ages may be different. Therefore, this issue should be evaluated in different research designs.

Moreover, we strongly encourage examining the effect of this kind of exercise on different patient groups. We tested adaptation of healthy cartilage. In animal models, researches showed that intact cartilage is more durable than impaired articular cartilage. Therefore, we do not have enough evidence to recommend the impact exercise for patients according to the findings of our study.

Effect of endurance type exercises are evaluated in this study. Effect of speed, strength or concurrent strength-endurance fitness activities will be significant in further studies since concurrent fitness programs have become popular for general health in recent years.

In this study, we used biochemical markers to observe changes in articular cartilage. Another important recommendation for further researchers is that findings about structural changes in articular cartilage will be reinforced by morphological examination like MR imaging.

REFERENCES

Aisen, A. M., McCune, W. J., MacGuire, A., Carson, P. L., Silver, T. M., Jafri, S. Z., et al. (1984). Sonographic evaluation of the cartilage of the knee. *Radiology*, *153*(3), 781-784.

American College of Sports Medicine (ACSM), (2001). *Guidelines for Exercise Testing and Prescription,* Johnson, E.P., Lippincott, Williams and Wilkins. Baltimore, Pp: 137-164.

Andersson, M. L. E., Thorstensson, C. A., Roos, E. M., Petersson, I. F., Heinegård, D., & Saxne, T. (2006). Serum levels of cartilage oligomeric matrix protein (COMP) increase temporarily after physical exercise in patients with knee osteoarthritis. *BMC Musculoskeletal Disorders*, *7*, 98. doi: 10.1186/1471-2474-7-98

Austin, G., & Noble, J. (1994). *Swimming for fitness* (2nd ed.). London A & C Black.

Backhaus, M., T. Kamradt, D. Sandrock, D. Loreck, J. Fritz, K. J. Wolf, et al. (1999). Arthritis of the finger joints: A comprehensive approach comparing conventional radiography, scintigraphy, ultrasound, and contrast-enhanced magnetic resonance imaging. *Arthritis & Rheumatism*, *42*(6), 1232-1245. doi: 10.1002/1529-0131(199906)42:6<1232::AID-ANR21>3.0.CO;2-3

Baechle, T. R., & Earle, R. W. (2000). *Essentials of strength training and conditioning* (2nd ed.). Champaign, IL: Human Kinetics.

Baliunas, A. J., Hurwitz, D. E., Ryals, A. B., Karrar, A., Case, J. P., Block, J. A., et al. (2002). Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *10*(7), 573-579.

Barker, M. K., & Seedhom, B. B. (1997). Articular cartilage deformation under physiological cyclic loading--apparatus and measurement technique. Journal *of Biomechanics,* 30(4), 377-381.

Bennell, K. L., Malcolm, S. A., Brukner, P. D., Green, R. M., Hopper, J. L., Wark, J. D., et al. (1998). A 12-month prospective study of the relationship between stress fractures and bone turnover in athletes. *Calcified Tissue International*, *63*(1), 80-85.

Bennell, K. L., Malcolm, S. A., Khan, K. M., Thomas, S. A., Reid, S. J., Brukner, P. D., et al. (1997). Bone mass and bone turnover in power athletes, endurance athletes, and controls: a 12-month longitudinal study. *Bone*, *20*(5), 477-484.

Biswal, S., Hastie, T., Andriacchi, T. P., Bergman, G. A., Dillingham, M. F., & Lang, P. (2002). Risk factors for progressive cartilage loss in the knee: a longitudinal magnetic resonance imaging study in forty-three patients. *Arthritis and Rheumatism*, *46*(11), 2884-2892. doi: 10.1002/art.10573

Bjarnason, N. H., & Christiansen, C. (2000). Early response in biochemical markers predicts long-term response in bone mass during hormone replacement therapy in early postmenopausal women. *Bone*, *26*(6), 561-569. doi: 10.1016/S8756-3282(00)00272-6

Bompa, T. O (1999). *Periodization: Theory and methodology of training* (4th ed.) Champaign, IL: Human Kinetics.

Brommer, H., Brama, P. A. J., Laasanen, M. S., Helminen, H. J., van Weeren, P. R., & Jurvelin, J. S. (2005). Functional adaptation of articular cartilage from birth to maturity under the influence of loading: a biomechanical analysis. *Equine Veterinary Journal*, *37*(2), 148-154.

Bruce, R. A., Kusumi, F., & Hosmer, D. (1973). Maximal oxygen intake and nomographic assessment of functional aerobic impairment in cardiovascular disease. *American Heart Journal, 85*(4), 546-562.

Bucksch, J. (2005). Physical activity of moderate intensity in leisure time and the risk of all cause mortality. *British Journal of Sports Medicine, 39*(9), 632-638. doi: 10.1136/bjsm.2004.015768

Carmichael, C., & Burke, E. R (1994). *Fitness cycling*. Champaign, IL: Human Kinetics.

Carter, D. R., & Wong, M. (2003). Modelling cartilage mechanobiology. *Philosophical Transactions of the Royal Society of London. Series B, Biological Sciences*, *358*(1437), 1461-1471. doi: 10.1098/rstb.2003.1346

Cavill, N., Kahlmeier, S., & Racioppi, F. (2006). *Physical activity and health in Europe* (s. 47). Copenhagen,World Health Organization (WHO) Regional Office for Europe.

Charni, N., Juillet, F., & Garnero, P. (2005). Urinary type II collagen helical peptide (HELIX-II) as a new biochemical marker of cartilage degradation in patients with osteoarthritis and rheumatoid arthritis. *Arthritis and Rheumatism*, *52*(4), 1081-1090. doi: 10.1002/art.20930

Christgau, S., Garnero, P., Fledelius, C., Moniz, C., Ensig, M., Gineyts, E., et al. (2001). Collagen type II C-telopeptide fragments as an index of cartilage degradation. *Bone*, *29*(3), 209-215.

Cohen, Z. A., McCarthy, D. M., Kwak, S. D., Legrand, P., Fogarasi, F., Ciaccio, E. J., et al. (1999). Knee cartilage topography, thickness, and contact areas from MRI: in-vitro calibration and in-vivo measurements. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *7*(1), 95-109. doi: 10.1053/joca.1998.0165

Creighton, D. L., Morgan, A. L., Boardley, D., & Brolinson, P. G. (2001). Weight-bearing exercise and markers of bone turnover in female athletes. *J Appl Physiol*, *90*(2), 565-570.

Cochrane, T., Davey, R. C., & Matthes Edwards, S. M. (2005). Randomised controlled trial of the cost-effectiveness of water-based therapy for lower limb osteoarthritis. *Health Technology Assessment (Winchester, England),* 9(31), iii-iv, ix-xi, 1-114.

Crnkic, M., Månsson, B., Larsson, L., Geborek, P., Heinegård, D., & Saxne, T. (2003). Serum cartilage oligomeric matrix protein (COMP) decreases in rheumatoid arthritis patients treated with infliximab or etanercept. *Arthritis Research & Therapy*, *5*(4), R181-185. doi: 10.1186/ar760

Darwin, C. (1872). The Origin of Species, 6th edit. New York: New America Library.

de Assis, M. A., de Mello, M. F., Scorza, F. A., Cadrobbi, M. P., Schooedl, A. F., da Silva, S. G., et al. (2008). Evaluation of physical activity habits in patients with posttraumatic stress disorder. *Clinics (São Paulo, Brazil), 63*(4), 473-478.

de Jong, Z., Munneke, M., Vilim, V., Zwinderman, A. H., Kroon, H. M., Ronday, H. K., et al.,(2008). Value of serum cartilage oligomeric matrix protein as a prognostic marker of large-joint damage in rheumatoid arthritisdata from the RAPIT study. *Rheumatology,* 47(6), 868-871. doi: 10.1093 /rheumatology/ken052.

Ding, C., Garnero, P., Cicuttini, F., Scott, F., Cooley, H., & Jones, G. (2005). Knee cartilage defects: association with early radiographic osteoarthritis, decreased cartilage volume, increased joint surface area and type II collagen breakdown. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *13*(3), 198-205. doi: 10.1016/j.joca.2004.11.007

Dolezal, B. A., & Potteiger, J. A. (1998). Concurrent resistance and endurance training influence basal metabolic rate in nondieting individuals. *Journal of Applied Physiolog, 85*(2), 695-700.

Duryea, J., Li, J., Peterfy, C. G., Gordon, C., & Genant, H. K. (2000). Trainable rule-based algorithm for the measurement of joint space width in digital radiographic images of the knee. *Medical Physics, 27*(3), 580-591.

Duryea, J., Zaim, S., & Genant, H. (2003). New radiographic-based surrogate outcome measures for osteoarthritis of the knee. *OSTEOARTHRITIS AND CARTILAGE*, *11*(2), 102-110. doi: 10.1053/joca.2002.0866

Eckstein, F., Faber, S., Mühlbauer, R., Hohe, J., Englmeier, K., Reiser, M., et al. (2002). Functional adaptation of human joints to mechanical stimuli. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *10*(1), 44-50. doi: 10.1053/joca.2001.0480

Eckstein, F., Gavazzeni, A., Sittek, H., Haubner, M., Lösch, A., Milz, S., et al. (1996). Determination of knee joint cartilage thickness using three-dimensional magnetic resonance chondro-crassometry (3D MR-CCM). *Magnetic Resonance in Medicine: Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, *36*(2), 256-265.

Eckstein, F., Hudelmaier, M., & Putz, R. (2006). The effects of exercise on human articular cartilage. *Journal of Anatomy*, *208*(4), 491-512. doi: 10.1111/j.1469-7580.2006.00546.x

Eckstein, F., Lemberger, B., Gratzke, C., Hudelmaier, M., Glaser, C., Englmeier, K., et al. (2005). In vivo cartilage deformation after different types of activity and its dependence on physical training status. *Annals of the Rheumatic Diseases*, *64*(2), 291-295. doi: 10.1136/ard.2004.022400

Eckstein, F., Lemberger, B., Stammberger, T., Englmeier, K. H., & Reiser, M. (2000). Patellar cartilage deformation in vivo after static versus dynamic loading. *Journal of Biomechanics*, *33*(7), 819-825.

Eckstein, F., Tieschky, M., Faber, S., Englmeier, K. H., & Reiser, M. (1999). Functional analysis of articular cartilage deformation, recovery, and fluid flow following dynamic exercise in vivo. *Anatomy and Embryology*, *200*(4), 419-424.

Eckstein, F., Tieschky, M., et al. (1998). Effect of physical exercise on cartilage volume and thickness in vivo: MR imaging study. *Radiology*, *207*(1), 243-248.

Eckstein, F., Westhoff, J., et al. (1998). In vivo reproducibility of three-dimensional cartilage volume and thickness measurements with MR imaging. *AJR. American Journal of Roentgenology*, *170*(3), 593-597.

Eckstein, F., & Glaser, C. (2004). Measuring cartilage morphology with quantitative magnetic resonance imaging. *Seminars in Musculoskeletal Radiology*, *8*(4), 329-353. doi: 10.1055/s-2004-861579

Everts, V., & Buttle, D. J. (2008). Methods in studying ECM degradation. *Methods (San Diego, Calif.), 45*(1), 86-92. doi: 10.1016/j.ymeth.2008.01.009

Faber, S. C., Eckstein, F., Lukasz, S., Mühlbauer, R., Hohe, J., Englmeier, K. H., et al. (2001). Gender differences in knee joint cartilage thickness, volume and articular surface areas: assessment with quantitative three-dimensional MR imaging. *Skeletal Radiology*, *30*(3), 144-150.

Foley, S., Ding, C., Cicuttini, F., & Jones, G. (2007). Physical activity and knee structural change: a longitudinal study using MRI. *Medicine and Science in Sports and Exercise*, *39*(3), 426-434. doi: 10.1249/mss.0b013e31802d97c6

Forsblad d'Elia, H., Christgau, S., Mattsson, L., Saxne, T., Ohlsson, C., Nordborg, E., et al. (2004). Hormone replacement therapy, calcium and vitamin D3 versus calcium and vitamin D3 alone decreases markers of cartilage and bone metabolism in rheumatoid arthritis: a randomized controlled trial [ISRCTN46523456]. *Arthritis Research & Therapy*, *6*(5), R457-468. doi: 10.1186/ar1215

Forslind, K., Eberhardt, K., Jonsson, A., & Saxne, T. (1992). Increased serum concentrations of cartilage oligomeric matrix protein. A prognostic marker in early rheumatoid arthritis. *British Journal of Rheumatology*, *31*(9), 593-598.

Fox, E. L., Bowers, R. W., & Foss, M. L. (1988). *Physiological Basis of Physical Education and Athletics* (4th ed.).Dubuque, Brown & Benchmark.

Fredriksen, P. M., Ingjer, F., Nystad, W., & Thaulow, E. (1998). Aerobic endurance testing of children and adolescents--a comparison of two treadmill-protocols. *Scandinavian Journal of Medicine & Science in Sports, 8*(4), 203-207.

Fukuda, Y., Takai, S., Yoshino, N., Murase, K., Tsutsumi, S., Ikeuchi, K., et al. (2000). Impact load transmission of the knee joint-influence of leg alignment and the role of meniscus and articular cartilage. *Clinical Biomechanics (Bristol, Avon)*, *15*(7), 516-521.

Garnero, P., Conrozier, T., Christgau, S., Mathieu, P., Delmas, P. D., & Vignon, E. (2003). Urinary type II collagen C-telopeptide levels are increased in patients with rapidly destructive hip osteoarthritis. *Annals of the Rheumatic Diseases*, *62*(10), 939-943.

Garnero, P., Piperno, M., Gineyts, E., Christgau, S., Delmas, P. D., & Vignon, E. (2001). Cross sectional evaluation of biochemical markers of bone, cartilage, and synovial tissue metabolism in patients with knee osteoarthritis: relations with disease activity and joint damage. *Annals of the Rheumatic Diseases*, *60*(6), 619-626.

Garnero, P., Rousseau, J. C., & Delmas, P. D. (2000). Molecular basis and clinical use of biochemical markers of bone, cartilage, and synovium in joint diseases. *Arthritis and Rheumatism*, *43*(5), 953-968. doi: 10.1002/1529-0131(200005)43:5<953::AID-ANR1>3.0.CO;2-Q

Garnero, P., Landewé, R., Boers, M., Verhoeven, A., Van Der Linden, S., Christgau, S., et al. (2002). Association of baseline levels of markers of bone and cartilage degradation with long-term progression of joint damage in patients with early rheumatoid arthritis: the COBRA study. *Arthritis and Rheumatism*, *46*(11), 2847-2856. doi: 10.1002/art.10616

Garnero, P., Sornay-Rendu, E., Arlot, M., Christiansen, C., & Delmas, P. D. (2004a). Association between spine disc degeneration and type II collagen degradation in postmenopausal women: the OFELY study. *Arthritis and Rheumatism*, *50*(10), 3137-3144. doi: 10.1002/art.20493

Gehlsen, G. M., Grigsby, S. A., & Winant, D. M. (1984). Effects of an aquatic fitness program on the muscular strength and endurance of patients with multiple sclerosis. *Physical Therapy, 64*(5), 653-657.

Giannoni, P., Siegrist, M., Hunziker, E. B., & Wong, M. (2003). The mechanosensitivity of cartilage oligomeric matrix protein (COMP). *Biorheology*, *40*(1-3), 101-109.

Gordon, N. F. (1993). *Arthritis: your complete exercise guide* . Champaign, IL : Human Kinetics.

Gök, H., Ergin, S., & Yavuzer, G. (2002). Kinetic and kinematic characteristics of gait in patients with medial knee arthrosis. *Acta Orthopaedica Scandinavica*, *73*(6), 647-652. doi: 10.1080/000164702321039606

Gratzke, C., Hudelmaier, M., Hitzl, W., Glaser, C., & Eckstein, F. (2007). Knee cartilage morphologic characteristics and muscle status of professional weight lifters and sprinters: a magnetic resonance imaging study. *The American Journal of Sports Medicine*, *35*(8), 1346-1353. doi: 10.1177 /0363546507299746

Hall, B.K. (2005). *Bones and cartilage: developmental and evolutionary skeletal biology.* San Diego, Calif: Elsevier Academic Press.

Hedbom, E., Antonsson, P., Hjerpe, A., Aeschlimann, D., Paulsson, M., Rosa-Pimentel, E., et al. (1992). Cartilage matrix proteins. An acidic oligomeric protein (COMP) detected only in cartilage. *The Journal of Biological Chemistry*, *267*(9), 6132-6136.

Henderson, J. H., de la Fuente, L., Romero, D., Colnot, C. I., Huang, S., Carter, D. R., et al. (2007). Rapid growth of cartilage rudiments may generate perichondrial structures by mechanical induction. *Biomechanics and Modeling in Mechanobiology*, *6*(1-2), 127-137. doi: 10.1007/s10237-006-0038-x

Hohe, J., Ateshian, G., Reiser, M., Englmeier, K., & Eckstein, F. (2002). Surface size, curvature analysis, and assessment of knee joint incongruity with MRI in vivo. *Magnetic Resonance in Medicine: Official Journal of the Society of Magnetic Resonance in Medicine / Society of Magnetic Resonance in Medicine*, *47*(3), 554-561.

Hohmann, E., Wörtler, K., & Imhoff, A. B. (2004). MR imaging of the hip and knee before and after marathon running. *The American Journal of Sports Medicine*, *32*(1), 55-59.

Housh, T.J., Housh, D.J. & DeVries, H.A. (2003). Applied exercise and sport physiology. Scottsdale, Arizona: Holcomb Hathaway, Publishers, Inc.

Hoshino, A., & Wallace, W. A. (1987). Impact-absorbing properties of the human knee. *The Journal of Bone and Joint Surgery. British Volume*, *69*(5), 807-811.

Hunter, D. J., March, L., & Sambrook, P. N. (2003). The association of cartilage volume with knee pain. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *11*(10), 725-729.

Hunter, D., Li, J., LaValley, M., Bauer, D., Nevitt, M., DeGroot, J., et al. (2007). Cartilage markers and their association with cartilage loss on magnetic resonance imaging in knee osteoarthritis: the Boston Osteoarthritis Knee Study. *Arthritis Research & Therapy*, *9*(5), R108. doi: 10.1186/ar2314

Hunter, D. J., & Eckstein, F. (2009). Exercise and osteoarthritis. *Journal of Anatomy*, *214*(2), 197-207. doi: 10.1111/j.1469-7580.2008.01013.x

Inoue, M., Yamamoto, S., Kurahashi, N., Iwasaki, M., Sasazuki, S., & Tsugane, S. (2008). Daily total physical activity level and total cancer risk in men and women: results from a large-scale population-based cohort study in Japan. *American Journal of Epidemiology, 168*(4), 391-403. doi: 10.1093/aje/kwn146.

Ito, K., Kimura, Y., Tajika, A., Fuchioka, S., Iwasaka, T., Nishiyama, T. (2007). Ultrasonographic changes of the knee joint cartilage associated with physical characterization in middle aged women: 6-month observational survey. *J. Phys.Ther. Sci.,19,* 277-282.

Jordan, J. M., Luta, G., Stabler, T., Renner, J. B., Dragomir, A. D., Vilim, V., et al. (2003). Ethnic and sex differences in serum levels of cartilage oligomeric matrix protein: the Johnston County Osteoarthritis Project. *Arthritis and Rheumatism*, *48*(3), 675-681. doi: 10.1002/art.10822

Karlsson, M. K., Nordqvist, A., & Karlsson, C. (2008). Sustainability of exercise-induced increases in bone density and skeletal structure. *Food & Nutrition Research, 52*. doi: 10.3402/fnr.v52i0.1872

Katz, J., & Bruning, N. (1993). *Swimming for total fitness: a progressive aerobic program* (2nd ed.). New York: Doubleday.

Kersting, U. G., Stubendorff, J. J., Schmidt, M. C., & Brüggemann, G. (2005). Changes in knee cartilage volume and serum COMP concentration after running exercise. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *13*(10), 925-934. doi: 10.1016/j.joca.2005.06.005

Kessler, M. A., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. B. (2006). Volume changes in the menisci and articular cartilage of runners: an in vivo investigation based on 3-D magnetic resonance imaging. *The American Journal of Sports Medicine*, *34*(5), 832-836. doi: 10.1177/0363546505282622

Kessler, M. A., Glaser, C., Tittel, S., Reiser, M., & Imhoff, A. B. (2008). Recovery of the menisci and articular cartilage of runners after cessation of exercise: additional aspects of in vivo investigation based on 3-dimensional magnetic resonance imaging. *The American Journal of Sports Medicine*, *36*(5), 966-970. doi: 10.1177/0363546507313093

Kim, H. J., Lee, Y. H., & Kim, C. K. (2007). Biomarkers of muscle and cartilage damage and inflammation during a 200 km run. *European Journal of Applied Physiology*, *99*(4), 443-447. doi: 10.1007/s00421-006-0362-y

Kim, H. J., Lee, Y. H., & Kim, C. K. (2009). Changes in serum cartilage oligomeric matrix protein (COMP), plasma CPK and plasma hs-CRP in relation to running distance in a marathon (42.195 km) and an ultra-marathon (200 km) race. *European Journal of Applied Physiology*, *105*(5), 765-770. doi: 10.1007/s00421-008-0961-x

Kiviranta, I., Tammi, M., Jurvelin, J., Säämänen, A. M., & Helminen, H. J. (1988). Moderate running exercise augments glycosaminoglycans and thickness of articular cartilage in the knee joint of young beagle dogs. *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society*, *6*(2), 188-195. doi: 10.1002/jor.1100060205

Konstantaki, M., Trowbridge, E. A., & Swaine, I. L. (1998). The relationship between blood lactate and heart rate responses to swim bench exercise and women's competitive water polo. *Journal of Sports Sciences, 16*(3), 251-256.

Koo, S., & Andriacchi, T. P. (2007). A comparison of the influence of global functional loads vs. local contact anatomy on articular cartilage thickness at the knee. *Journal of Biomechanics*, *40*(13), 2961-2966. doi: 10.1016/j.jbiomech.2007.02.005

Kuettner, K. E., Goldberg, V. M., & Surgeons, A. A. O. O. (1995). *Osteoarthritic disorders: workshop, Monterey, California, April 1994*. Rosemont, IL: The Academy.

Kühne, S. A., Neidhart, M., Everson, M. P., Häntzschel, H., Fine, P. R., Gay, S., et al. (1998). Persistent high serum levels of cartilage oligomeric matrix protein in a subgroup of patients with traumatic knee injury. *Rheumatology International*, *18*(1), 21-25.

Lammi, M. J., Häkkinen, T. P., Parkkinen, J. J., Hyttinen, M. M., Jortikka, M., Helminen, H. J., et al. (1993). Adaptation of canine femoral head articular cartilage to long distance running exercise in young beagles. *Annals of the Rheumatic Diseases*, *52*(5), 369-377.

Lang, P., Noorbakhsh, F., & Yoshioka, H. (2005). MR imaging of articular cartilage: current state and recent developments. *Radiologic Clinics of North America*, *43*(4), 629-639, vii. doi: 10.1016/j.rcl.2005.02.009

Lang, T. F. (2006). What do we know about fracture risk in long-duration spaceflight? *Journal of Musculoskeletal & Neuronal Interactions*, *6*(4), 319-321.

Larsson, E., Erlandsson Harris, H., Lorentzen, J. C., Larsson, A., Månsson, B., Klareskog, L., et al. (2002). Serum concentrations of cartilage oligomeric matrix protein, fibrinogen and hyaluronan distinguish inflammation and cartilage destruction in experimental arthritis in rats. *Rheumatology (Oxford, England)*, *41*(9), 996-1000.

LeBlanc, A. D., Spector, E. R., Evans, H. J., & Sibonga, J. D. (2007). Skeletal responses to space flight and the bed rest analog: a review. *Journal of Musculoskeletal & Neuronal Interactions*, *7*(1), 33-47.

Lee, I. M., Rexrode, K. M., Cook, N. R., Manson, J. E., & Buring, J. E. (2001). Physical activity and coronary heart disease in women: is "no pain, no gain" passé? *JAMA: The Journal of the American Medical Association*, *285*(11), 1447-1454.

Leon, A. S., Myers, M. J., & Connett, J. (1997). Leisure time physical activity and the 16-year risks of mortality from coronary heart disease and all-causes in the Multiple Risk Factor Intervention Trial (MRFIT). *International Journal of Sports Medicine*, *18 Suppl 3*, S208-215.

Lester, M. E., Urso, M. L., Evans, R. K., Pierce, J. R., Spiering, B. A., Maresh, C. M., et al. (2009). Influence of exercise mode and osteogenic index on bone biomarker responses during short-term physical training. *Bone*. doi: 10.1016/j.bone.2009.06.001

Lieber, D. C., Lieber, R. L., & Adams, W. C. (1989). Effects of run-training and swim-training at similar absolute intensities on treadmill VO_2max. *Medicine and Science in Sports and Exercise*, *21*(6), 655-661.

Lin, S. Y., Davey, R. C., & Cochrane, T. (2004). Community rehabilitation for older adults with osteoarthritis of the lower limb: a controlled clinical trial. *Clinical Rehabilitation*, *18*(1), 92-101.

Lindsey, C. T., Narasimhan, A., Adolfo, J. M., Jin, H., Steinbach, L. S., Link, T., et al. (2004). Magnetic resonance evaluation of the interrelationship between articular cartilage and trabecular bone of the osteoarthritic knee. *Osteoarthritis and Cartilage*, *12*(2), 86-96. doi: 10.1016/j.joca.2003.10.009

Lu, X. L., & Mow, V. C. (2008). Biomechanics of articular cartilage and determination of material properties. *Medicine and Science in Sports and Exercise*, 40(2), 193-199. doi: 10.1249/mss.0b013e31815cb1fc.

MacAuley, D. (1994). A history of physical activity, health and medicine. Journal of the Royal Society of Medicine, 87(1), 32-35.

Maglischo, E. W., & Brennan, C. F. (1985). *Swim for the health of it*. Palo Alto : Mayfield Pub. Co.

Mühlbauer, R., Lukasz, T. S., Faber, T. S., Stammberger, T., & Eckstein, F. (2000). Comparison of knee joint cartilage thickness in triathletes and physically inactive volunteers based on magnetic resonance imaging and three-dimensional analysis. *The American Journal of Sports Medicine*, *28*(4), 541-546.

Mündermann, A., Dyrby, C. O., Hurwitz, D. E., Sharma, L., & Andriacchi, T. P. (2004). Potential strategies to reduce medial compartment loading in patients with knee osteoarthritis of varying severity: reduced walking speed. *Arthritis and Rheumatism*, *50*(4), 1172-1178. doi: 10.1002/art.20132

Mündermann, A., Dyrby, C. O., & Andriacchi, T. P. (2005). Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis and Rheumatism*, *52*(9), 2835-2844. doi: 10.1002/art.21262

Mündermann, A., Dyrby, C. O., Andriacchi, T. P., & King, K. B. (2005). Serum concentration of cartilage oligomeric matrix protein (COMP) is sensitive to physiological cyclic loading in healthy adults. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *13*(1), 34-38. doi: 10.1016/j.joca.2004.09.007

Mündermann, A., Dyrby, C. O., D'Lima, D. D., Colwell, C. W., & Andriacchi, T. P. (2008). In vivo knee loading characteristics during activities of daily living as measured by an instrumented total knee replacement. *Journal of Orthopaedic Research: Official Publication of the Orthopaedic Research Society*, *26*(9), 1167-1172. doi: 10.1002/jor.20655

Neidhart, M., Hauser, N., Paulsson, M., DiCesare, P. E., Michel, B. A., & Häuselmann, H. J. (1997). Small fragments of cartilage oligomeric matrix protein in synovial fluid and serum as markers for cartilage degradation. *British Journal of Rheumatology*, *36*(11), 1151-1160.

Neidhart, M., Müller-Ladner, U., Frey, W., Bosserhoff, A. K., Colombani, P. C., Frey-Rindova, P., et al. (2000). Increased serum levels of non-collagenous matrix proteins (cartilage oligomeric matrix protein and melanoma inhibitory activity) in marathon runners. *Osteoarthritis and Cartilage*, *8*(3), 222-229. doi: 10.1053/joca.1999.0293

Niehoff, A., Kersting, U., Helling, S., Dargel, J., Maurer, J., Thevis, M., et al. (2008). Elevation of serum cartilage oligomeric matrix protein (comp) level depends on loading mode of physical activity – preliminary results. *Journal of Biomechanics*, *41*, S116-S116. doi: 10.1016/S0021-9290(08)70116-7

Nishimura, K., Tanabe, T., Kimura, M., Harasawa, A., Karita, K., & Matsushita, T. (2005). Measurement of articular cartilage volumes in the normal knee by magnetic resonance imaging: can cartilage volumes be estimated from physical characteristics? *Journal of Orthopaedic Science: Official Journal of the Japanese Orthopaedic Association*, *10*(3), 246-252. doi: 10.1007/s00776-005-0889-5

O'Kane, J. W., Hutchinson, E., Atley, L. M., & Eyre, D. R. (2006). Sport-related differences in biomarkers of bone resorption and cartilage degradation in endurance athletes. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *14*(1), 71-76. doi: 10.1016/j.joca.2005.08.003

Paffenbarger, R. S., Blair, S. N., & Lee, I. (2001). A history of physical activity, cardiovascular health and longevity: the scientific contributions of Jeremy N Morris, DSc, DPH, FRCP. *Int. J. Epidemiol.*, *30*(5), 1184-1192. doi: 10.1093/ije/30.5.1184

Petersson, I. F., Boegård, T., Saxne, T., Silman, A. J., & Svensson, B. (1997). Radiographic osteoarthritis of the knee classified by the Ahlbäck and Kellgren & Lawrence systems for the tibiofemoral joint in people aged 35-54 years with chronic knee pain. *Annals of the Rheumatic Diseases, 56*(8), 493-496.

Pocock, N. A., Eisman, J. A., Hopper, J. L., Yeates, M. G., Sambrook, P. N., & Eberl, S. (1987). Genetic determinants of bone mass in adults. A twin study. *The Journal of Clinical Investigation*, *80*(3), 706-710. doi: 10.1172/JCI113125

Potter, H. G., Linklater, J. M., Allen, A. A., Hannafin, J. A., & Haas, S. B. (1998). Magnetic resonance imaging of articular cartilage in the knee. An evaluation with use of fast-spin-echo imaging. *The Journal of Bone and Joint Surgery. American Volume*, *80*(9), 1276-1284.

Qi, C., & Changlin, H. (2007). Levels of biomarkers correlate with magnetic resonance imaging progression of knee cartilage degeneration: a study on canine. *Knee Surgery, Sports Traumatology, Arthroscopy: Official Journal of the ESSKA*, *15*(7), 869-878. doi: 10.1007/s00167-006-0280-x

Qi, C., Changlin, H., & Zefeng, H. (2007). Matrix metalloproteinases and inhibitor in knee synovial fluid as cartilage biomarkers in rabbits: the effect of high-intensity jumping exercise. *The Journal of Surgical Research*, *140*(1), 149-157. doi: 10.1016/j.jss.2006.12.556

Racunica, T. L., Teichtahl, A. J., Wang, Y., Wluka, A. E., English, D. R., Giles, G. G., et al. (2007). Effect of physical activity on articular knee joint structures in community-based adults. *Arthritis and Rheumatism*, *57*(7), 1261-1268. doi: 10.1002/art.22990

Raissouni, N., Gossec, L., Ayral, X., & Dougados, M. (2005). New concepts in the diagnosis and treatment of recent-onset polyarthritis. *Joint, Bone, Spine: Revue Du Rhumatisme*, *72*(2), 119-123. doi: 10.1016/j.jbspin.2004.04.009

Raynauld, J., Martel-Pelletier, J., Berthiaume, M., Labonté, F., Beaudoin, G., de Guise, J. A., et al. (2004). Quantitative magnetic resonance imaging evaluation of knee osteoarthritis progression over two years and correlation with clinical symptoms and radiologic changes. *Arthritis and Rheumatism*, *50*(2), 476-487. doi: 10.1002/art.20000

Roos, E. M., & Dahlberg, L. (2005). Positive effects of moderate exercise on glycosaminoglycan content in knee cartilage: a four-month, randomized, controlled trial in patients at risk of osteoarthritis. *Arthritis and Rheumatism*, *52*(11), 3507-3514. doi: 10.1002/art.21415

Salari, S., Wu, H., Webber, C., Fuentes, C.O., Ogilvie R.A., Bobba, R., et al. (2008). Can vibration analysis be used to evaluate knee osteoarthritis? *Osteoarthritis and Cartilage, 16*(supp. 4), S129.

Salci, Y., Tansel, B., Celik, O., Karakaya, H., Sarioglu, T., Korkusuz F. (2001). Relationship Between Bone Mineral Density and Physical Activity Level of Active and Sedentary Women Between 19-40yrs. Old. *Hacettepe Journal of Sport Sciences, 12*(2), 3-8.

Scharhag-Rosenberger, F., Meyer, T., Walitzek, S., & Kindermann, W. (2009). Time course of changes in endurance capacity: a 1-yr training study. *Medicine and Science in Sports and Exercise, 41*(5), 1130-1137. doi: 10.1249 /MSS.0b013e3181935a11

Seedhom, B. B., & Wallbridge, N. C. (1985). Walking activities and wear of prostheses. *Annals of the Rheumatic Diseases*, *44*(12), 838-843.

Setton, L. A., Elliott, D. M., & Mow, V. C. (1999). Altered mechanics of cartilage with osteoarthritis: human osteoarthritis and an experimental model of joint degeneration. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *7*(1), 2-14. doi: 10.1053/joca.1998.0170

Sharif, M., Kirwan, J. R., Elson, C. J., Granell, R., & Clarke, S. (2004). Suggestion of nonlinear or phasic progression of knee osteoarthritis based on measurements of serum cartilage oligomeric matrix protein levels over five years. *Arthritis and Rheumatism*, *50*(8), 2479-2488. doi: 10.1002/art.20365

Stitik, T. P., Gazzillo, G., & Foye, P. M. (2007). State of the Art Review: Osteoarthritis and Therapeutic Exercise. *American Journal of Lifestyle Medicine*, *1*(5), 360-366. doi: 10.1177/1559827607303245.

Swaine, I. L. (1997). Time course of changes in bilateral arm power of swimmers during recovery from injury using a swim bench. *British Journal of Sports Medicine, 31*(3), 213-216.

Swaine, I. L. (2000). Arm and leg power output in swimmers during simulated swimming. Medicine and Science in Sports and Exercise, 32(7), 1288-1292.

Taaffe, D. R., Robinson, T. L., Snow, C. M., & Marcus, R. (1997). High-impact exercise promotes bone gain in well-trained female athletes. *Journal of Bone and Mineral Research: The Official Journal of the American Society for Bone and Mineral Research*, *12*(2), 255-260.

Taskiran, D. (2007). [Biochemical markers in cartilage injury and repair]. *Acta Orthopaedica Et Traumatologica Turcica*, *41 Suppl 2*, 6-12.

Tomiya, M., Fujikawa, K., Ichimura, S., Kikuchi, T., Yoshihara, Y., & Nemoto, K. (2009). Skeletal unloading induces a full-thickness patellar cartilage defect with increase of urinary collagen II CTx degradation marker in growing rats. *Bone*, *44*(2), 295-305. doi: 10.1016/j.bone.2008.10.038

U.S. Department of Health and Human Services. Physical Activity and Health: A Report of the Surgeon General. Atlanta, GA: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 1996.

Vanwanseele, B., Eckstein, F., Knecht, H., Spaepen, A., & Stüssi, E. (2003). Longitudinal analysis of cartilage atrophy in the knees of patients with spinal cord injury. *Arthritis and Rheumatism*, *48*(12), 3377-3381. doi: 10.1002/art.11367

Vanwanseele, B., Eckstein, F., Knecht, H., Stüssi, E., & Spaepen, A. (2002). Knee cartilage of spinal cord-injured patients displays progressive thinning in the absence of normal joint loading and movement. *Arthritis and Rheumatism*, *46*(8), 2073-2078. doi: 10.1002/art.10462

Vanwanseele, B., Lucchinetti, E., & Stüssi, E. (2002). The effects of immobilization on the characteristics of articular cartilage: current concepts and future directions. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *10*(5), 408-419. doi: 10.1053/joca.2002.0529

Vilím, V., Olejárová, M., Machácek, S., Gatterová, J., Kraus, V. B., & Pavelka, K. (2002). Serum levels of cartilage oligomeric matrix protein (COMP) correlate with radiographic progression of knee osteoarthritis. *Osteoarthritis and Cartilage / OARS, Osteoarthritis Research Society*, *10*(9), 707-713.

Viton J.-M., Timsit M., Mesure S., Granier P., Franceschi J.-P., Delarque A., et al. (1998). Gait analysis in knee arthritis patients. *Journal of Biomechanics*, *31*, 47. doi: 10.1016/S0021-9290(98)80096-1

Vosse, D., Landewé, R., Garnero, P., van der Heijde, D., van der Linden, S., & Geusens, P. (2008). Association of markers of bone- and cartilage-degradation with radiological changes at baseline and after 2 years follow-up in patients with ankylosing spondylitis. *Rheumatology (Oxford, England)*, *47*(8), 1219-1222. doi: 10.1093/rheumatology/ken148

Whipple, T. J., Le, B. H., Demers, L. M., Chinchilli, V. M., Petit, M. A., Sharkey, N., et al. (2004). Acute effects of moderate intensity resistance exercise on bone cell activity. *International Journal of Sports Medicine*, *25*(7), 496-501. doi: 10.1055/s-2004-820942

Wijayaratne, S. P., Teichtahl, A. J., Wluka, A. E., Hanna, F., Bell, R., Davis, S. R., et al. (2008). The determinants of change in patella cartilage volume--a cohort study of healthy middle-aged women. *Rheumatology (Oxford, England)*, *47*(9), 1426-1429. doi: 10.1093/rheumatology/ken244

Williams, F., & Spector, T. (2008). Biomarkers in osteoarthritis. *Arthritis Research & Therapy*, *10*(1), 101. doi: 10.1186/ar2344.

Williams, F. M. K., Andrew, T., Saxne, T., Heinegard, D., Spector, T. D., & MacGregor, A. J. (2006). The heritable determinants of cartilage oligomeric matrix protein. *Arthritis and Rheumatism*, *54*(7), 2147-2151. doi: 10.1002 /art.21931

Wisłowska, M., & Jabłońska, B. (2005). Serum cartilage oligomeric matrix protein (COMP) in rheumatoid arthritis and knee osteoarthritis. *Clinical Rheumatology*, *24*(3), 278-284. doi: 10.1007/s10067-004-1000-x

Wong, P. C. H., Chia, M. Y. H., Tsou, I. Y. Y., Wansaicheong, G. K. L., Tan, B., Wang, J. C. K., et al. (2008). Effects of a 12-week exercise training programme on aerobic fitness, body composition, blood lipids and C-reactive protein in adolescents with obesity. *Annals of the Academy of Medicine, Singapore, 37*(4), 286-293.

Wong, M., & Carter, D. R. (2003). Articular cartilage functional histomorphology and mechanobiology: a research perspective. *Bone*, *33*(1), 1-13. doi: 10.1016/S8756-3282(03)00083-8

Zhang, W. (2008). OARSI recommendations for the management of hip and knee osteoarthritis, Part II: OARSI evidence-based, expert consensus guidelines. *Osteoarthritis Cartilage*, *16*(2), 137-62.

APPENDICES

A. INFORMED CONSENT FORM

AYDINLATILMIŞ ONAM FORMU

Bu çalışmanın amacı 12 hafta süre ile üç farklı türde, fakat benzer süre ve şiddetlerde egzersiz yapan yetişkin erkeklerin Elisa yöntemi ile kandaki COMP oranına bakılarak kıkırdak deformasyonunun karşılaştırılması ve kıkırdak dokusunun, yapılan akut fiziksel egzersize karşı adaptasyon gelişiminin karşılaştırılmasıdır. Oluşan değişiklikler biyokimyasal işaretciler kullanılarak gözlemlenecektir. Bu çalışmanın sonuçları, literatürde eksik kalan düzenli egzersiz ve kıkırdak yapısı arasındaki ilişkiyi ortaya koyacaktır. Literatürde yer alan çalışmalarda göze çarpan eksikliklerden: tek grupla yapılan veya tek tip egzersizle yapılan kesitsel çalışmalarda eksik kalan farklı antrenman türlerinin ve adaptasyonun etkisi bu çalışma ile doldurulacaktır.
Testler ODTÜ, Sağlık ve Rehberlik Merkezi laboratuvarlarında gerçekleştirilecektir. Katılımcılar 7 farklı teste ilk-test ve son-test olmak üzere 12 hafta ara ile toplam 2 kez girecek olup ölçümler yaklaşık 4 saat sürecektir. Ölçümlerde VO_2max, İzokinetik kuvvet, eklem pozisyon algılaması, iki farklı turde vücut kompozisyonu, kemik mineral yoğunlugu, esneklik ve kanda kıkırdak isaretleyicilerini inceleyen tesler yapılacaktır.
Bu araştırmada ölçülecek olan saptanacak olan kemik mineral kaybının belirtileri erken yaşlarda alınması gereken önlemlerle ilgili size rehber olacaktır. Ayrıca araştırmanın bulguları başka insanların yararına kullanılabilir.
Yukarıda yer alan ve araştırmadan önce gönüllüye verilmesi gereken bilgileri gösteren Aydınlatılmış Onam Formu adlı metni kendi anadilimde okudum ya da bana okunmasını sağladım. Bu bilgilerin içeriği ve anlamı, yazılı ve sözlü olarak açıklandı. Aklıma gelen bütün soruları sorma olanağı tanındı ve sorularıma doyurucu cevaplar aldım. Çalışmaya katılmadığım ya da katıldıktan sonra çekildiğim durumda, hiçbir yasal hakkımdan vazgeçmiş olmayacağım. Bu koşullarla, söz konusu araştırmaya hiçbir baskı ve zorlama olmaksızın gönüllü olarak katılmayı kabul ediyorum. Bu metnin imzalı bir kopyasını aldım.

Gönüllünün Adı- Soyadı:
Yaş ve Cinsiyeti:
İmzası:
Adresi (varsa telefon ve/veya fax numarası):
Tarih:
Açıklamaları Yapan Araştırmacı- Hekimin
Adı- Soyadı:
İmzası:
Görevi:
Tarih:

B: ETHIC COMMITY APPROVAL

T.C.
MUSTAFA KEMAL ÜNİVERSİTESİ
Tayfur Ata Sökmen Tıp Fakültesi Dekanlığı
Etik Kurul Başkanlığı

BÜRO : Özel Kalem
SAYI : B.30.2.MKÜ.0.01.01.00/ 255
KONU : Etik Kurul Kararları

08/02/2007

Sayın
Yrd.Doç.Dr.Aydıner KALACI
Ortopedi ve Travmatoloji AD

Fakültemiz Etik Kurulunun 06/02/2007 ve 2 sayılı toplantısında alınan 2 ve 3 nolu karar örnekleri aşağıya çıkartılmıştır.

Bilgilerinizi ve gereğini rica ederim.

Prof.Dr.Ertuğrul EĞİLMEZ
Dekan V.

KARAR 2- Fakültemiz Cerrahi Tıp Bilimleri Bölümü Ortopedi ve Travmatoloji Anabilim Dalı öğretim üyesi Yrd.Doç.Dr.Aydıner KALACI'nın "Ortopedist Gözüyle Orak Hücreli Anemi ve Talesemi" isimli çalışması incelenerek Etik Kurallara uygun olduğuna katılanların oy birliği ile karar verilmiştir.

KARAR 3- Fakültemiz Cerrahi Tıp Bilimleri Bölümü Ortopedi ve Travmatoloji Anabilim Dalı öğretim üyesi Yrd.Doç.Dr.Aydıner KALACI'nın "Farklı Karakterdeki Branşlarda Egzersiz Yapan Sedanterlerde 12 Haftalık Egzersizin Eklem Kıkırdağına Etkileri" isimli çalışması incelenerek Etik Kurallara uygun olduğuna katılanların oy birliği ile karar verilmiştir.

C. DATA COLLECTION SHEET

Date : .... /.... / 2007

Group **S** ☐ **C** ☐ **R** ☐ **Co** ☐

Name, Surname :

Weight :

Height :

Date of Birth :

Dominant Leg :

Lower Extremity Injury : Yes ☐ No ☐

Resting Heart Rate :

Supine Blood Pressure :

D. VO_2max EVALUATION SHEET

PERFORMANS TEST BULGULARI

Last Name:	[redacted]	First Name:	[redacted]
Identification:	205-30	Date of Birth:	11.03.1985
Sex:	male	Height:	172,0 cm
Weight:	75,0 kg	Age:	22 Years
Rel. Weight:	104 %	BSA:	1,88 m²
BMI:		Free text:	

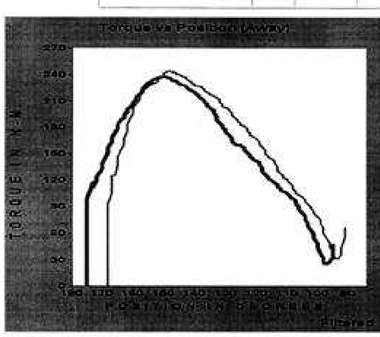
Summary		AT %VO2m	AT	Marker No. 17	Last Resting load	MaxVO2
Time averaging 5 Seconds						
Time	min					14:05
VTex	L					2.843
VTin	L					2.724
t-tot	s					1.11
t-ex	s					0.556
t-in	s					0.55
FICO2	%					-
FIO2	%					20.88
SpO2	%					75
FECO2	%					3.86
FETCO2	%					5.42
FEO2	%					17.62
FETO2	%					16.31
V'CO2	ml/min					4344
V'O2	ml/min					3481
VO2/kg	ml/min/kg					46.4
O2/HR	ml					0.0
BF	1/min					54
V'E	L/min					154
RER						1.25
O2 deb	ml					0.00
O2 def	ml					0.00
dO2/dW	ml/min/Watt					11.55
t-ph	min					11:07
St Slo	V/s					0
PECO2	kPa					3.25
PETCO2	kPa					4.57
PEO2	kPa					14.85
PETO2	kPa					13.74
EqCO2						33.1
EqO2						41.3
BR	%					-
Lac	mmol/L					0.0

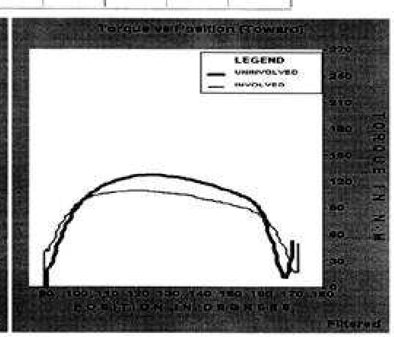
E. ISOKINETIC STRENGTH EVALUATION SHEET

Comprehensive Evaluation

Name:	[redacted]	Session:	21.05.2007 17:29:38	Windowing:	**None**
ID:	**205-28**	Involved:	**None**	Protocol:	**Isokinetic Bilateral**
Birth Date:	(dd.MM.yyyy)	Clinician:		Pattern:	**Extension/Flexion**
Ht:		Referral:		Mode:	**Isokinetic**
Wt:	**79.0**	Joint:	**Knee**	Contraction:	**CON/CON**
Gender:	**Male**	Diagnosis:		GET:	**18 N-M at 90 Degrees**

		EXTENSION 60 DEG/SEC			FLEXION 60 DEG/SEC		
# OF REPS: Right 5		UNINVOLVED	INVOLVED	DEFICIT	UNINVOLVED	INVOLVED	DEFICIT
# OF REPS: Left 5		RIGHT	LEFT		RIGHT	LEFT	
PEAK TORQUE	N-M	237.6	243.4	-2.4	126.8	109.1	14.0
PEAK TQ/BW	%	300.7	308.1		160.5	138.0	
TIME TO PK TQ	MSEC	420.0	340.0		580.0	490.0	
ANGLE OF PK TQ	DEG	150.0	148.0		124.0	118.0	
TORQ @ 30.0 DEG	N-M	0.0	0.0	0.0	0.0	0.0	0.0
TORQ @ 0.18 SEC	N-M	188.1	219.2	-16.5	92.2	92.4	-0.2
COEFF. OF VAR.	%	6.3	7.3		6.8	2.2	
MAX REP TOT WORK	J	222.2	236.2	-6.3	138.1	130.6	5.4
MAX WORK REP #	#	5	3		1	1	
WRK/BODYWEIGHT	%	281.3	299.1		174.8	165.3	
TOTAL WORK	J	1018.9	1088.7	-6.8	650.8	596.9	8.3
WORK FIRST THIRD	J	355.9	385.5		242.5	219.7	
WORK LAST THIRD	J	315.4	333.2		183.4	182.2	
WORK FATIGUE	%	11.4	13.6		24.4	17.1	
AVG. POWER	WATTS	152.5	160.6	-5.3	96.3	86.9	9.8
ACCELERATION TIME	MSEC	20.0	20.0		40.0	30.0	
DECELERATION TIME	MSEC	60.0	40.0		40.0	30.0	
ROM	DEG	85.2	86.1		85.2	86.1	
AVG PEAK TQ	N-M	220.8	227.7		119.2	105.1	
AGON/ANTAG RATIO	%	53.4	44.8	G: 61.0			





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F. TÜRKÇE ÖZET

FARKLI DARBELERDEKİ EGZERSİZLERİN EKLEM KIKIRDAĞININ DEFORMASYONEL DAVRANIŞINA VE FONKSİYONEL ADAPTASYONUNA ETKİSİ

Giriş

Yaklaşık 140 yıl önce, ünlü biyolog Charles Darwin (1872) dokuların, yapılarını çevresel etkilere karşı koruyabilmelerini veya geliştirme becerilerini "Fonksiyonel Adaptasyon" olarak adlandırmıştı. Bu adaptasyon, merkezi sinir sisteminde ve iç organlarda ortaya çıkabileceği gibi, mekanik görevler üstlenen kemik ve kas dokularında da gözlenmektedir (Eckstein, Hudelmaier, & Putz, 2006).

Kıkırdak dokusu da kemik ve kas dokuları gibi, bedenin gerçekleştirdiği hareketlere bağlı olarak, ağırlık taşımakta veya çarpmalara maruz kalmaktadır. Günlük döngüsel hareketler insanların en çok alt ekstemitelerinde yük oluşturmaktadır ve bu bölgedeki eklemler yılda ortalama bir ilâ dört milyon kez vucüt ağırlığını taşıyacak döngüsel hareket gerçekleştirmektedir (Barker & Seedhom, 1997; Seedhom & Wallbridge, 1985). Yapılan düzenli sportif aktivtelerle bu rakamların daha da artacağı açıktır. Bu kadar yüksek oranda fiziksel etkiye maruz kalmasına rağmen, insan kıkırdağının fiziksel egzersizlere olan reaksiyonları son zamanlara kadar yeterince araştırılmamıştı. Günümüze kadar, bu konuda en popüler araştırmalar hayvan çalışmaları ile sınırlı kalmış, insan kıkırdağının egzersize göstermiş olduğu cevapları araştıran çalışmalar oldukça sınırlı sayıda kalmıştı.

Kıkırdak dokusunun fonksiyonel adaptasyonu ile ilgili çalışmaların kısıtlı kalmasının temel sebepleri eklemlerin karmaşık yapısı ve kıkırdak değerlendirme yöntemlerinin kolay uygulanamaması ve ölçüm hassasiyetinin yeterince gelişmemiş olması idi. Fakat günümüzde kıkırdak dokusunun morfolojik yapısını ve değişimlerini oldukça güvenilir şekilde gösteren magnetik rezonans görüntüleme teknikleri ve yapısal değişimlerini gösteren son derece geçerli ve güvenilir biyokimyasal işaretleyiciler geliştirilmiştir. Bu yenilikler sayesinde, günümüzde artikular kıkırdakta oluşan yapısal ve morfolojik değişimleri hassas şekilde belirlemek mümkün hale gelmiştir.

Bu yeni değerlendirme metodlarını kullanarak yapılan güncel çalışmalar genellikle artrit hastalarında egzersiz tavsiyelerinin etkinliğini değerlendirmek üzere yapılmış çalışmalardan oluşmaktadır (Gordon, 1993; Zhang ve ark., 2008). Bu tavsiyeler hastalara düzenli olarak yapılan aerobik dayanıklılık, kas kuvveti ve esnekliği geliştirici çalışmaları önermektedir. Benzer tavsiyeler genel sağlığın korunması ve iyileştirilmesi için de önerilmiştir (ACSM, 2001; Cavill, Kahlmeier & Racioppi, 2006). Tüm bu tavsiyelerde koşu, bisiklet ve yüzme hem genel sağlıkta hem de osteoartritlilerin rehabilitasyonunda en çok ismi geçen egzersiz türleri olarak göze çarpmaktadır.

Sonuç olarak, farklı süre, şiddet veya sıklıkta yapılansa bile bu tür egzersizler halk sağlığı ve osteoartritlilerin rehabilitasyonu için tavsiye edilmektedir, fakat bu egzersizlerin sağlıklı insan kıkırdağına etkileri net olarak ortaya konulamamıştır. Önceki çalışmalar, hayvan modelleri, kadavra değerlendir-meleri veya sporcu gruplarının farklarını ortaya koymak ile sınırlı kalmıştır. Bu çalışma, genel sağlık için en sık tavsiye edilen egzersiz türlerinin aynı şiddet, hacim ve sıklıkta uygulandığında insan diz eklem kıkırdağında oluşturduğu degişiklikleri ortaya çıkarmak üzere tasarlandı.

Bu amaçla iki temel konu sorgulandı:

1. 12 hafta süre ile düzenli olarak yapılan ve diz ekleminde farklı seviyelerde çarpma etkisi oluşturan üç farklı spor dalının diz kıkırdağının deformasyonel davranışına etkisi nedir?
2. 12 hafta süre ile düzenli olarak yapılan ve diz ekleminde farklı seviyelerde çarpma etkisi oluşturan üç farklı spor dalının diz kıkırdağının fonksiyonel adaptasyonuna etkisi nedir?

Materyal ve Metod

Bu çalışma, 12 hafta süre ile düzenli olarak yapılan yüksek ve orta çarpma etkisi oluşturan ve hiç çarpma etkisi oluştumayan fiziksel egzersizlerin diz eklem kıkırdağının deformasyonel davranışına ve fonksiyonel adaptasyonuna olan etkisini araştırmak üzere planlandı.

Konunun araştırılması için randomize kontrollü bir araştırma tasarımı kullanıldı. Bu çalışmaya toplam 48 sağlıklı erkek katılımcı ile başlandı. Katılımcıların yaşları 19-25 arasıydı. Katılımcılar çalışmada gönüllü olarak yer aldı. Bu katılımcıların 36 tanesi egzersiz grubu, 12 tanesi ise kontrol grubunda yer aldı. Katılımcılarda aranan genel özellikler; sağlıklı erkek olmaları, sedanter bir yaşam tarzlarının olması ve spor geçmişlerinin olmamasıydı. Çalışmaya katılımı engelleyen kriterler; osteoartrit, romatoidartrit gibi inflamatuvar hastalığı olmaları, son altı ayda alt ektremitelerde kemik kırığı yaşamış olmaları ve ilaç veya alkol bağımlısı olmalarıydı. İki katılımcı çalışmanın egzersiz periyodunda, iki katılımcı da biyokimyasal analizler sırasında çalışmadan çıkarıldı.

Tüm katılımcılar çalışmanın başında ve sonunda bir dizi teste tabi tutuldular. Tüm testler Orta Doğu Teknik Üniversitesi laboratuvarlarında gerçekleştirildi. Testler fiziksel uygunluk testleri ve kıkırdak değerlendirme testleriydi.

Ön-testlerin ardından egzersiz grubunda yer alan 36 katılımcı rastgele örneklem yöntemi ile eşit üç gruba ayrıldı. Bu gruplar: yüksek çarpma etkisine sahip koşu egzersizi yapacak grup, orta seviyede çarpma etkisine yaratan bisiklet egzersizi yapacak grup ve diz ekleminde çarpma etkisi yaratmayan yüzme egzersizi yapacak gruptu.

Tüm egzersiz grupları, her seansı 40 dakika süren, haftada üç günlük egzersiz programlarına 12 hafta süreyle düzenli olarak katıldılar. 40 dakikalık egzersiz seansları, 5 dakika ısınma, 30 dakika ana set ve 5 dakika soğuma evrelerinden oluştu. Egzersizlerin içeriği American College of Sport Medicine's (ACSM) kılavuzlarında belirtilen kriterlere göre düzenlendi (ACSM, 2001) ve egzersizin şiddeti Karvonen formülü kullanılarak her katılımcının bireysel kalp atım hızı rezervinin %60-70'inde yapılacak şekilde ayarlandı (Bompa, 1999, syf.87). Yüzme egzersizleri olimpik yüzme havuzunda, koşu ve bisiklet egzersizleri ise laboratuvar ortamında koşubandı ve bisiklet ergometresi üzerinde yapıldı. Egzersizler süresince kalp atım hızları kaydedildi. 12 haftalık egzersiz uygulaması süresince kontrol grubu herhangi bir sportif faaliyete katılmadı, ayrıca günlük faaliyetlerine herhangi bir kısıtlama getirilmedi.

12 haftalık antrenman periyodunun ardından son-testler uygulandı ve tüm katılımcılar ön-testlerde uygulanan fiziksel uygunluk ölçümlerine ve kıkırdak değerlendirme ölçümlerine tekrar tabi tutuldular.

Katılımcıların fiziksel uygunluk değerlendirmeleri, vucüt kitle indeksleri (VKİ), maksimum oksijen kullanma kapasiteleri (VO_2max) ve maksimum izokinetik kuvvetleri ölçülerek ve 12 hafta sonunda bu parametrelerdeki değişimler karşılaştırılarak yapıldı. Vucüt kitle indeksi, vucüt ağırlığının, boyun karesine bölünmesiyle hesaplandı (Heyward & Stolarczyk 1996). Katılımcıların VO_2max'ı standart Bruce protokolü (Bruce, Kusumi & Hosmer 1973) uygulanarak, VIASYS Healthcare ergospirometry line, the MasterScreen CPX (Wuerzburg, Almanya) sistemleri ile direk olarak ölçüldü. VO_2max değerleri ml/kg/dak cinsinden ifade edildi. İzokinetik kuvvet ölçümleri Biodex Sistem Dinamometresi (Biodex Medical Inc, Shirley, NY) kullanılarak ölçüldü. Katılımcılar dominant bacakları ile 60 ^{o}/sn lik açısal hızla toplam beş tane bükülme ve düzelme hareketi gerçekleştirdiler. Ölçümlerde kuadriseps kas grubunun ulaştığı en yüksek torkun vucüt ağırlığına oranı (PT/VA) maximum izokinetik kuvvet olarak kabul edildi.

Katılımcıların kıkırdak yapılarında oluşan değişimler, biyokimyasal osteoartrit isaretleyicilerinden kıkırdağa özel Kıkırdak Oligomerik Matriks Protein (KOMP) ve kemiğe özel Tip-I kollagenin C-terminal Telopeptidlerin (CTX-I) kullanılarak değerlendirildi. Bu işaretleyicilerin kandaki yogunluklarının farklı yorgunluk ve dinlenme seviyelerinde, ön ve son testlerdeki değişimleri karşılaştırıldı. Kan alım ve işleme prosedürü Munderman'dan (2005) modifiye edildi.

Katılımcılar kan testlerine gelmeden 48 saat önce fiziksel olarak yorucu olan faaliyetlere ara verdiler. Kan testine gelen katılımcılar 15 dakika sandalyede oturarak dinlendi. Ardından katılımcılara orta şiddette yarım saatlik yürüme egzersizi yaptırıldı. Bu egzersizin hemen öncesinde, hemen sonrasında ve yarım saatlik oturarak dinlenme sonrasında 5 mililitre venöz kan örneği alındı. Serumu ayrıştırılan kan örnekleri biyokimyasal analizler yapılana kadar -80°C' de korundu.

Biyokimyasal işaretleyicilerin konsantrasyonları özel bir enstitüde ELİSA yöntemi kulanılarak analiz edildi. Bu analizlerde KOMP ve CTX-I konsantrasyon değerlendirmeleri biyokimyasal kitlerin üreticisi olan kuruluşların belirttiği prosedürlere uygun olarak gerçekleştirildi (sırasıyla, COMP® ELISA; AnaMar Medical AB, Lund, İsveç ve Serum CrossLaps® ELISA; Immunodiagnostic Systems Nordic A/S, Herlev, Danimarka).

İstatistiksel analizler SPSS programı kullanılarak yapıldı. Toplanan fiziksel uygunluk ve biyokimyasal verileri ayrı ayrı 4x2 (grup ve zaman) “mixed repeated measures ANOVA” tasarımı ile test edildi. Post-hoc testler Bonferroni düzeltmeli eşleştirilmiş *t* testi kullanılarak yapıldı.

Sonuçlar

Fiziksel ölçüm sonuçları, katılımcıların her grupta benzer özelliklere sahip olduğunu göstermiştir. Tüm katılımcıları sağlıklı genç erkekler olan bu çalışmada VKİ’ler tüm gruplarda normal sınırlar içinde yer almaktaydı. 12 hafta süresince koşu grubunun antrenmanlara katılımı %86, bisiklet grubunun %84, yüzme grubunun ise %90 dı.

Normal aralıkta yer alan VKİ değerlerinde 12 hafta antrenman programı sonunda tüm egzersiz gruplarında anlamlı seviyede düşüş gözlendi ($p < 0.05$). Ayrıca dayanıklılık performansı ölçümleri, düzenli dayanıklılık egzersizlerinin oksijen kullanma kapasitesini anlamlı olarak geliştirdiğini gösterdi ($p < 0.05$). 12 hafta sonunda koşu grubunda VO_2max değerleri 10.6%, bisiklet grubunda 6.2%, yüzme grubunda ise 12.0% arttığı gözlemlendi. Kontrol grubunda ise VKİ ve VO_2max değerlerinde anlamlı bir farklılığa rastlanmadı. İzokinetik kuvvet ölçümleri, 12 haftalık dayanıklılık türü egzersizin sadece yüzme grubunda kuvvet değerlerini anlamlı olarak artırdığını gösterdi ($p < 0.05$).

KOMP verilerinin analizi yarım saatlik yürüme egzersizinin, sağlıklı genç sedanter erkeklerin diz eklem kıkırdağında deformasyonel bir davranışa sebep olduğunu gösterdi ($p < 0.05$). 12 haftalık egzersiz sonunda yarım saatlik yürüme egzersizinin yüksek çarpma etkisine sahip koşu egzersizi yapan grupta artık deformasyonel bir davranışa sebep olamadığı gözlemlendi ($p < 0.05$).

CTX-I verilerinin analizi yarım saatlik yürüme egzersizinin, sağlıklı genç sedanter erkeklerin kemiğe özel osteortrit işaterleyicisi olan CTX-I konsantrasyonuna etki etmediğini gösterdi. Ayrıca, 12 haftalık egzersiz sonunda da yarım saatlik yürüme egzersizinin hiçbir grupta CTX-I birikimine sebep olmadığı gözlemlendi.

Tartışma

Egzersiz gruplarında yer alan katılımcılar 12 hafta süresince ACSM tavsiyeleri doğrultusunda dayanıklılık egzersizleri yaptı. Bu egzersizlerin tamamı devinimsel hareketlerden oluşan aerobik tipte egzersizlerdi fakat diz ekleminde oluşturdukları çarpma etkisi biribirinden farklıydı.

Çalışmanın sonuçları, tüm egzersiz türlerinin VKİ değerlerini düşürdüğünü, VO_2max değerlerini ise arttırdığını gösterdi. İzokinetik kuvvet ise sadece yüzme grubunda arttı. Bu bulgular, 12 hafta süreyle yapılan egzersizin, sporun fiziksel uygunluk parametreleri üzerindeki etkilerini genel olarak yansıtacak şekilde uygulandığını göstermektedir. VKİ ve VO_2max değerlerinde gözlemlenen değişimler kısmen fonksiyonel adaptasyonla açıklanabilir (Darwin, 1872). Bu bulgular güncel literatürle de paralellik göstermektedir. Çok yeni bir çalışmada, Kindermann (2009) bizim tasarımımıza benzeyen bir araştırmada 12 haftalık düzenli aerobik egzersizin bazı fiziksel uygunluk parametrelerine etkisini araştırmıştır. Kindermann çalışmasında yaptığı ara ölçümlerde, VO_2max değerlerinde anlamlı bir artışa üçüncü ayda ulaşıldığını, vucüt ağırlığının ise altıncı ayda anlamlı olarak düştüğünü gözlemlemiştir. Benzer bir çalışmada Lieber, Lieber, & Adams (1989) 11.5 hafta süre ile yapılan koşu ve yüzme egzersizinin koşu bandı üzerinde yapılan VO_2max testine olan etkisini araştırmışlardır. Bu çalışmada da araştırmacılar bizim çalışmamızda olduğu gibi yaklaşık 12 haftalık antrenmanın VO_2max değerini anlamlı olarak artırdığını gözlemlemişlerdir. Bu çalışmada tüm egzersiz grupları döngüsel hareketlerden oluşan dayanıklılık egzersizleri yaptılar. Dolayısıyla bu tür bir antrenman programının, izokinetik kuvvetin artışına sebep olması her zaman beklenen bir bulgu değildi. Bu tür bir adaptasyon su sporlarının doğasında bulunan izokinetik benzeri akuatik dirence karşı yapılan egzersizin sebep olduğu bir gelişim olarak değerlendirilebilir. İzokinetik kas kasılması özel olarak tasarlanmış makinalarla oluşturulabilen bir direnç türü olmakla beraber Fox, Bowers, & Foss'e (1988) göre doğada isokinek kasılmaya benzer verilebilecek en iyi örneklerden birisi yüzme hareketindeki kulaçlardır. Yüzme grubunda gözlenen izokinetik kuvvetteki artışın bu benzerlikten kaynaklanmış olabileceği düşünülmektedir.

Ön-testlerde yarım saatlik egzersizin, sağlıklı genç sedanter erkeklerin serum KOMP konsantrasyonlarını anlamlı olarak artırdığı gözlemlendi. Bu bulgu literatürle paralellik bir bulgudur. Akut koşu egzersizinin serum KOMP konsantrasyonunu anlamlı olarak artırdığını Kersting ve arkadaşları (2005) daha önce belirtmişlerdi. Aynı yıl Mundermann ve ekibi (2005) daha hafif bir egzersiz olan günlük yürüme hızında yarım saatlik egzersizin bile serum KOMP konsantrasyonunu anlamlı olarak artırdığını gözlemlemişlerdir.

Ayrıca, akut egzersizin kıkırdağın morfolojik yapısına olan etkileri de farklı araştırmacılar tarafından araştırılmıştır. Bu tür MR çalışmalarının bulguları, genellikle biyokimysal işaretleyici bulguları ile paralellik göstermektedir. Eckstein ve arkadaşları (1998) çok tekrarlı diz bükme hareketi yapan bireylerin MR görüntülerinde, kıkırdak kalınlığında geçici olarak anlamlı miktarda incelme olduğunu gözlemledi. Sonraki yıl, Eckstein ve arkadaşları (1999) yapılan farklı egzersizlerin ardından kıkırdak kalınlığının farklı miktarlarda inceldiğini ortaya koydu. Bu bulgu kıkırdakta gözlemlenen deformasyonel davranışın yapılan egzersizin çarpma dozuna göre değiştiğini de göstermektedir.

12 hafta sonunda yarım saatlik yürüyüş egzersizinin, yüksek çarpma etkisine sahip koşu egzersizi yapan grupta serum KOMP seviyesini, dolayısıyla kıkırdağın deformasyonel davranışını azalttığı gözlemlendi. Gözlemlenen bu değişim kıkır dokusunun fonksiyonel adaptasyonu olarak değerlendirilebilir. Literatürde eklem kıkırdağının fonksiyonel adaptasyonu ile ilgili ortak bir kanı yoktur.

Eklem kıkırdağının fonksiyonel adaptasyonu ile ilgili olarak ilk çalışmalar hayvan denekler üzerinde yapılan çalışmalardı. Kiviranta ve arkadaşlarının (1988) fiziksel egzersizin atlarda lokal olarak kıkırdak dokusunu nasıl etkilediğini araştırdıkları çalışmalarında en fazla adaptasyonun, eklemin yük taşıyan bölgelerinde meydana geldiğini gözlemlediler. İnsan deneklerle yapılan çalışmalar ise genellikle elit sporcuların eklem kıkırdak morfolojileri ile sedanter bireylerin eklem kıkırdaklarının karşılaştırılması yoluyla yapılmaya çalışıldı. Muhlbauer ve arkadaşları (2000) elit triatletlerin ortalama veya maksimum diz kıkırdak kalınlıklarının sedanter bireylerden anlamlı olarak farklı olmadığını gözlemledi. Fakat Muhlbauer'in araştırmasının ve benzeri çalışmaların zayıf yönü, elit sporcuların bu eklemlerinde meydana gelen aşırı yüklenmenin fonksiyonel adaptasyonun negatif yönde gelişme ihtimalini göz ardı etmeleriydi. Ayrıca elit sporcuların genetik yapılarından gelen farklılıklar kimi zaman antrenmanla değiştirilebilecek özelliklerden daha fazla belirleyici farklılıklar doğurabileceği göz önüne alınması gereken etkenlerdendir.

Bu araştırmacıların aksine, güncel çalışmalar bizim çalışmamızda ortaya konulan bilgileri doğrulamaktadır. Foley ve arkadaşları (2007) diz kıkırdak ekleminin dinamik bir yapı olduğunu ve fiziksel egzersize olumlu cevaplar verdiğini savunmuştu. Ayrıca Foley, kas kuvveti ve dayanıklılık antrenmanının kıkırdak kaybına karşı koruyucu etkisinin olduğunu savunmuştur. Ayrıca, boylamsal bir çalışmada Racunica ve arkadaşları (2007) şiddetli fiziksel aktvitelerin sakatlık geçmişi olmayan sağlıklı bireylerde kıkırdak sağlığı için faydalı olduğunu ortaya koymuşlardır.

Kemik dokusuna özel osteoartrit işaretleyicisi olan CTX-I verileri yarım saatlik yürüyüş egzersizinin, bu biyokimyasalın serumdaki artışını tetikleyecek şiddette veya sürede bir uyarıcı etkiye sahip olmadığını gösterdi. 12 haftalık egzersiz sonunda da CTX-I verileri ön testlerle paralel sonuçlar göstermiştir. Bu sabitliğin sebebi osteoartrit ve romatoid tedavisinin takibinde oldukça etkili olan CTX-I (Bjarnason & Christiansen, 2000) değerlendirmelerinin, sporla ilgili çalışmalarda yüksek standartlarda hassasiyete sahip olmadığıdır (Whipplle ve ark. 2004).

Sonuç ve Öneriler

Bu çalışmada, tüm egzersiz gruplarında dayanıklılık performansı anlamlı seviyede arttı ve katılımcılar daha yüksek oksijen kullanma kapasitesine ulaştılar. Ayrıca tüm egzersiz gruplarında VKİ değerleri anlamlı olarak düştü. Bu gelişmeler, düzenli olarak yapılan fiziksel egzersizlerin genel sağlık üzerine olumlu etkilerini göstermektedir.

Bu çalışmanın en önemli hipotezi, tüm diğer dokular gibi kıkırdak dokusunun da çevresel uyaranlara karşı fonksiyonel bir adaptasyon göstermesi idi. Ön-testlerde spor geçmişi olmayan katılımcıların diz eklem kıkırdağının yarım saatlik yürüyüş sonucunda deforme olduğu gözlenmiştir. Hipotezimizi sorgulamak için diz ekleminin hareketli olduğu 12 haftalık egzersizler uygulandı. Uygulanan bu programın sonucunda 30 dakikalık egzersizin diz eklemine en çok darbeyi oluşturan koşu grubunda artık deformasyona sebep olmadığı gözlemlendi. Bu bulgu, eklem kıkırdak dokusunun da fonksiyonel adaptasyon geliştirme yeteneğini ortaya koymaktadır.

Bu çalışmanın tüm bulguları düzenli olarak yapılan orta şiddet ve hacimdeki dayanıklılık egzersizlerinin, genel sağlığın geliştirilmesi için tavsiye edilebilecek nitelikler taşıdığını göstermektedir. Genel sağlık tavsiyelerine ek olarak, bu çalışmanın bulguları göstermektedir ki, vucüt ağırlığını taşıyarak yaptığımız egzersizler diz kıkırdak ekleminde fonksiyonel adaptasyon geliştirebilecek miktarda uyarı oluşturmaktadır. Bu tür egzersizlerin, genç erkekler için kıkırdak dokusunun yapısını güçlendiren bir etkiye sahip olduğu söylenebilir. Ayrıca, bu tür yüksek darbeli egzersizlerin, vücut ağırlığının taşınmadığı spor dallarında mücadele eden sporcuların kıkırdak sağlığı açısından, genel antrenman programlarının içerisinde yer ayrılması tavsiye edilebilir.

Bu çalışmanın sınırlılıkları sadece genç, sağlıklı, erkek katılımcılardan oluşması, sadece dayanıklılık antrenmanlarının uygulanması ve sadece yapısal değişimlerin değerlendirilmesi idi. Bu yüzden, ileride yapılacak çalışmaların farklı gruplarda, farklı antrenman türlerinin kıkırdakta oluşturduğu şekilsel ve yapısal değişimlerin değerlendirildiği çalışmalar olması tavsiye edilebilir.

G. CURRICULUM VITAE

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Date of Birth	May 08th, 1976
Place of Birth	Gürün
Marital Status	Married
Nationality	Turkish
Current Occupation	Research Assistant

Research interests:

Training theory and Endurance performance

Prevention and rehabilitation of sports injuries

Joint loading during sport activities

Adaptation and degeneration of cartilage under physiological conditions

Formal Education:

2003 - 2010	PhD. at Middle East Technical University - Physical Education and Sports Department
1999 - 2002	M.S. at Middle East Technical University - Physical Education and Sports Department
1995 - 1999	B.S. at Middle East Technical University - Physical Education and Sports Department

Languages:

Turkish	Native
English	Fluent

Professional Experience:

2000 - 2010	Middle East Technical University, Research Assistant
2000 - present	Middle East Technical University, Triathlon Team Coach
2009 - present	Middle East Technical University, Sports Club, Swimming Team Head Coach
2005 - 2008	Ekol Swimming and Triathlon Club, Swimming Team Head Coach
1998 - 2006	Middle East Technical University, Swimming Team Coach
2001 - 2002	Baskent University, Swimming Team Coach
2000 - 2001	Reyhan Swimming Specialization Sports Club, Swimming Team Coach
1999 - 2000	Mustafa Kemal University, Research Assistant
1994 - 1999	METU Swimming Pool, Swimming Teacher
1994 - 1999	METU Swimming Pool, Life Guard

Professional Activities and Qualifications:

2001	Coaching Certificate by the Turkish National Swimming Federation, Directorate General of Youth and Sports
1997	Life Saving Certificate Turkish Under Water Sports, Life-Saving, Water Ski and Fin Swimming Federation - Silver Sportsman
2003 - 2004	Member of Turkish Triathlon Federation Technical Council
2004 - 2008	National Team Coach of Turkish Triathlon Team
1998 - 2003	Member of Turkish National Triathlon Team
2002 - 2004	Member of Turkish Swimming Federation Education Council
2001 - 2003	Member of Turkish Triathlon Federation Education Council
2003 - 2004	Member of Turkish Triathlon Federation Technical Council

Teaching Experience:

Undergraduate Courses

4530213	Track and Field I
4530214	Track and Field II
4530225	General Physical Conditioning
4530307	Intermediate Swimming
4530331	Training Theory

Computer Skills:

Microsoft Office	All Microsoft Office applications
Program and Software	SPSS 15.0
	Lunar DPX pro, DXA system Software
	MasterScreen CPX gas analyzer Software
	Biodex isokinetic system, Advantage Software Rev. 3.27

Publications:

Papers Published in Refereed International Journals:

Ozdemir R.A., **Celik O.,** & Asci F.H (2009). Exercise interventions and their effects on physical self perceptions of male university students. International Journal of Psychology. (in-press).

Celik, O., Salcı, Y., Manisalı, M., & Korkusuz, F. (2009). The effect of hip rotation on bone mineral density of the proximal femur measured by dual energy X-ray absorptiometry. Joint Diseases & Related Surgery. 20(2): 71-77.

Tastan, M, **Celik, O.,** Weber G.W, Karasozen B, Korkusuz F. (2006). Mathematical modeling of proximal femur geometry and bone mineral density. Joint Diseases & Related Surgery. 17(3):128-136

Celik, O., Kosar N, Korkusuz F, Bozkurt M. (2005). Reliability and validity of the modified Conconi test on Concept II rowing ergometers. J Strength Cond Res;19:871-877

Bachev, V., Neykov, S., **Celik, O.,** Calupsis, S., Surucu, B. (2001). Comparative analysis of results of competitive rowing and 2000 M Concept II ergometer tests. Sport and Science *(Cnopt & Hayka).* 5, 140-146

Papers Published in Refereed National Journals:

Celik, O., Ince, M.L., Kirazci, S. (2002). A group of triathletes' physical, physiological and performance changes due to training: a four year longitudinal study. Hacettepe Journal of Sport Sciences. 8 (1), 17-24.

Salci, Y., Tansel, B., **Celik, O.,** Karakaya, H., Sarioglu, T., Korkusuz F. (2001). Relationship Between Bone Mineral Density and Physical Activity Level of Active and Sedentary Women Between 19-40yrs. Old. Hacettepe Journal of Sport Sciences. 12 (2), 3-8.

Celik, O., Kocak, S. (2001). Stroke Patterns and Swimming Times of Male Swimmers in 100M Events at 2000 University Games. Marmara Sports Research Review. 5 (2-3), 93-103.

International Congress and Presentations:

Celik, O., Y. Salci, F. Korkusuz, A. Kalaci. (2008). Changes in Serum Cartilage Oligomerıc Matrix Protein Concentration after 12 Weeks Impact or Non-Impact Exercises. 2008 World Congress on Osteoarthritis. Rome, Italy: 18-21 September.

Ozdemir, R.A., **Celik, O.,** Asci H.F. (2007). Effects of Different Exercise Interventions on Physical Self Perceptions and Some Physiological Parameters of Male University Students. International Mediterranean Sports Science Congress. Antalya, Turkey: 09-11 November.

Tastan M., **Celik O.,** Weber G.-W., Korkusuz F., Karasozen B. (2007) New Approaches in Mathematical Modeling of Proximal Femur Geometry and Bone Mineral Density. International Symposium on Health Informatics and Bioinformatics Turkey '07, HIBIT, Antalya, Turkey, (http://hibit.ii.metu.edu.tr/07/index.html) 30 April - 2 May.

Avsar, P.A., **Celik, O.,** Korkusuz F. (2005). The Effect of Different Cycling Cadence on Knee Joint Proprioception in Triathletes. The 46th ICHPER.SD Anniversary World Congress. Istanbul, Turkey: 9-13 November.

Coskun, O. O., Ozberk, Z.N., Salci, Y., **Celik, O.,** Altun, O., Akin, S., Bayramoglu, A., Korkusuz, F. (2005). Evaluation of Physiological Characteristics of Elite Basketball Players. The 46th ICHPER.SD Anniversary World Congress. Istanbul, Turkey: 9-13 November.

Celik, O., Kosar S. N., Korkusuz F. (2002). Reliability and Validity of Modified Conconi Test on Rowing Ergometers. 7th International Sports Sciences Congress. Antalya, Turkey: 27-29 October.

Bachev, V., Calupsis, S., Diafas V., **Celik, O.** (2002). Optimum Results of Visual Feedback of Some Rowing Ergometer Tests. 7th. Annual Congress of the European Collage of Sport Science. Athens, Greece: 24-28 July.

Bachev, V., İnce M.L., Tuzun M., **Celik, O.,** Agascioglu E., Surucu B., Neykov, S., Calupsis, S. (2002). The Analysis of Interval Training Content and Ergometer Performances of a Group of Rowers. National Sports Academy, Anniversary Scientific Conference. Sofia, Bulgaria

Bachev, V., **Celik, O.,** Calupsis, S., Sürücü, B. (2001). Comparative Analysis of Results of Competitive Rowing and 2000 M Concept II Ergometer Tests. Balkan Scientific Conference. Sofia, Bulgaria: 25-26 April.

Celik, O., Kocak S. (2000). The Effect of Stroke Patterns on Swimming Velocity. 6th International Sports Sciences Congress. Ankara, Turkey: 3-5 November.

Celik, O., Ince M.L., Kirazci, S. (2000). A Group of Triathletes' Physical, Physiological and Performance Changes Due To Training: A Four Year Longitudinal Study. 6th International Sports Sciences Congress. Ankara, Turkey: 3-5 November.

Salci, Y., Tansel, B., **Celik, O.,** Karakaya, H., Sarioglu, T., Korkusuz F. (2000). Comparison of Bone Mineral Density of Physically Active and Sedentary Women Between 19-40 Years Old. 6th International Sports Sciences Congress. Ankara, Turkey: 3-5 November.

National Congress and Presentations:

Sozeri, B., Kocak, S., **Celik, O.** (2009). Turkcell Süper Lig'teki Dört Büyük Futbol Kulübünün Online Promosyonel Aktivitelerinin İncelenmesi. III. Ulusal Futbol ve Bilim Kongresi, 9-11 Ocak, Antalya / Türkiye.

Projects:

2007	Kalaci A.., **O. Celik,** Y. Salci. The Investigation of Changes in Articular Cartilage and Blood Cartilage Parameters Among the Sedantery Men Related with 12-weeks Exercise. The Scientific and Technological Research Counsel of Turkey-107S112
2006	Korkusuz F., **O. Celik,** Y. Salci. Effects of Different Sports Background on Articular Cartilage on Recreational Athletes. BAP- 06-07-03-00-17
2005	Kocak, S., S. Yildirim, Y. Salci, **O. Celik**, M. Ücgül, S. Toker. Design and development project on web-based training theory course context. BAP-05-04-02
2001	Kirazci, S., **O. Celik**, F. Korkusuz & N. Kosar. Reliability and Validity of Modified Conconi Test on Rowing Ergometers. AFP-2001-05-04-03.

Awards:

14-18 Oct 2009	Free Communication, Young Investigator Award. European Federation of Sports Medicine Associations (EFSMA)
November 2009	The Scientific & Technological Research Council of Turkey. International publication encouragement award
October 2006	The Scientific & Technological Research Council of Turkey. International publication encouragement award

Current Participations:

14-18 Oct 2009	6th European Sports Medicine Congress, Antalya-Turkey
18-21 Sep 2008	World Congress on Osteoarthritis, Rome-Italy
18-20 April 2008	Clinical Orthopedics and Related Research, Writing Workshop, Istanbul-Turkey
16-25 June 2008	Head Coach of National Triathlon Team Camp for World University Triathlon Championship
26-30 June 2008	Technical Delegate of World University Triathlon Championship, Erdek-Turkey