Turk J Phys Med Rehab 2016;1(62):28-36
DOI: 10.5606/tftrd.2016.93899

Original Article / Özgün Araştırma

The effects of closed kinetic chain exercise on articular cartilage morphology: myth or reality? a randomized controlled clinical trial

Kapalı kinetik zincir egzersizinin kıkırdak morfolojisine etkileri: mit mi, gerçek mi? Randomize kontrollü klinik çalışma

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Received / *Geliş tarihi*: December 2014 Accepted / *Kabul tarihi*: April 2015

ABSTRACT

Objectives: This study aims to investigate the effects of kinetic chain exercises on the joint cartilage and to assess whether it is possible to repair cartilage in patients with grade 1-3 knee osteoarthritis (OA).

Patients and methods: Between December 2011 and May 2013, a total of 35 patients with grade 1-3 OA were included. The patients were randomly assigned into two groups as group 1 (exercise group, n=19) and group 2 (control group, n=16). The patients in group 1 performed closed kinetic chain exercises, transcutaneous electrical nerve stimulation (TENS) and hot-pack supervised by physiotherapists for three weeks in the hospital setting, followed by nine weeks of home exercises. The patients in group 2 were treated with TENS + hot-pack for three weeks. All patients were evaluated by magnetic resonance imaging at baseline and at week 12. The primary increase in the cartilage volume and thickness was analyzed. Both groups were also compared for pain and functionality.

Results: There was no significant differences in the pre- and post-treatment total cartilage volume (from 4594.73 mm^3 to 4866.80 mm^3) and medial and lateral tibial plateau cartilage thickness (from 2.06 mm to 2.10 mm, and from 2.30 mm to 2.35 mm, respectively) in group 1 ($p=0.505$, $p=0.450$, $p=0.161$, respectively). Similarly, no significant difference in the pre- and post-treatment cartilage volume and thickness between the groups was observed ($p>0.05$). In terms of functionality, there were significant differences between the exercise group and the control group ($p<0.05$).

Conclusion: Our study results show no significant effect of closed kinetic chain exercise on the cartilage volume or morphology.

Keywords: Exercise; knee cartilage; magnetic resonance imaging; osteoarthritis.

ÖZ

Amaç: Bu çalışmada kinetik zincir egzersizlerinin eklem kıkırdağı üzerindeki etkileri araştırıldı ve grad I-III diz osteoartriti (OA) olan hastalarda kıkırdak tamirinin mümkün olup olmadığı değerlendirildi.

Hastalar ve yöntemler: Aralık 2011 - Mayıs 2013 tarihleri arasında, grad I-III OA'lı toplam 35 hasta çalışmaya alındı. Hastalar grup 1 (egzersiz grubu, n=19) ve grup 2 (kontrol grubu, n=16) olmak üzere, rastgele iki gruba ayrıldı. Grup 1'deki hastalara hastanede fizyoterapistler gözetiminde üç hafta boyunca kapalı kinetik zincir egzersizleri, transkutanöz elektriksel sinir stimülasyonu (TENS) ve sıcak paket; ardından dokuz hafta boyunca ev egzersizi uygulandı. Grup 2'deki hastalar üç hafta süreyle TENS + sıcak paket ile tedavi edildi. Tüm hastalar başlangıçta ve 12. haftada manyetik rezonans görüntüleme yöntemi ile değerlendirildi. Kıkırdak hacmi ve kalınlığındaki başlıca artış analiz edildi. Her iki grup ağrı ve işlevsellik açısından da değerlendirildi.

Bulgular: Grup 1'de tedavi öncesi ve sonrası total kıkırdak hacmi (4594.73 mm^3'ten 4866.80 mm^3'e) ve medial ve lateral tibial plato kıkırdak kalınlığı (sırasıyla 2.06 mm'den 2.10 mm'ye, ve 2.30 mm'den 2.35 mm'ye) açısından anlamlı bir fark yoktu (sırasıyla, $p=0.505$, $p=0.450$, $p=0.161$). Benzer şekilde, gruplar arasında tedavi öncesi ve sonrası kıkırdak hacmi ve kalınlığı ($p>0.05$) açısından da anlamlı bir fark gözlenmedi ($p>0.05$). İşlevsellik açısından, egzersiz grubu ve kontrol grubu arasında da anlamlı bir farka rastlanmadı ($p<0.05$).

Sonuç: Çalışma sonuçlarımız, kapalı kinetik zincir egzersizlerinin kıkırdak hacmi veya morfolojisi üzerinde anlamlı bir etkisinin olmadığını göstermektedir.

Anahtar sözcükler: Egzersiz; diz kıkırdağı; manyetik rezonans görüntüleme; osteoartrit.

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Cite this article as:
Dinçer Ü, Arıbal S, Saygın H, İncedayı M, Rodop O. The effects of closed kinetic chain exercise on articular cartilage morphology: myth or reality? a randomized controlled clinical trial. Turk J Phys Med Rehab 2016;62:28-36.

Joint cartilage has limited healing and renewal capabilities. It is still believed that longitudinal damage to the joint cartilage tissue in adults cannot heal and that such damage can even worsen over time.[1,2] Unless cartilage damage is prevented or treated in time, the inevitable end result is osteoarthritis (OA).[3]

The main factor underlying the sustained function and structure of the joint cartilage is thought to be a reasonable mechanical load. Although mechanical joint functions are thought to affect the cartilage histomorphology and composition, the type of signal pathway which the mechanical load mobilizes within the cellular and extracellular matrices is unknown. Some loading features including magnitudes, directions, and loading time create a specific daily loading history for the joints and cartilages in each individual.[4]

Elastic deformation in the joint cartilage caused by mechanical load is a well-known condition. In addition, the fluid at the joint cartilage (on the surface or in the extracellular matrix) is displaced while walking or during exercise. Absorbed fluid helps to restore the cartilage.[5] Chondrocytes, the main type of cell in the joint cartilage, have mechanosensitive characteristics. Mechanical stimulation has been shown to enhance the biosynthetic activity of chondrocytes which detect physical loading and respond through the up or down regulation of the distinct gene sets.[6] Theses mechanosensitive genes includes collagens, aggrecans, growth proteins, interleukins (IL) 1, 4, and 6, matrix metalloproteinases, and some angiogenic and anti-angiogenic factors.[7,8] The chondrocytes interacts with their environment through dozens of types of membrane-bound receptors.[9] Another important factor is the extracellular matrix. Although the relationship between exercise and extracellular matrix still remains to be elucidated, the results of many studies performed on animals and data obtained from adolescents show that exercise increases the volume of joint cartilage.[10,11]

In this study, the impact of closed kinetic chain exercise on cartilage thickness and volume in individuals with OA (between 40 and 60 years of age) was examined. Several studies in the literature reported positive impacts of exercise on knee joint cartilage. There are also some evidences for thickening and volumetric increase on the osteoarthritic cartilage depending on the water retention and increasing glycosaminoglycan (GAG) contents. However, this is still controversial and the osteoarthritic cartilage

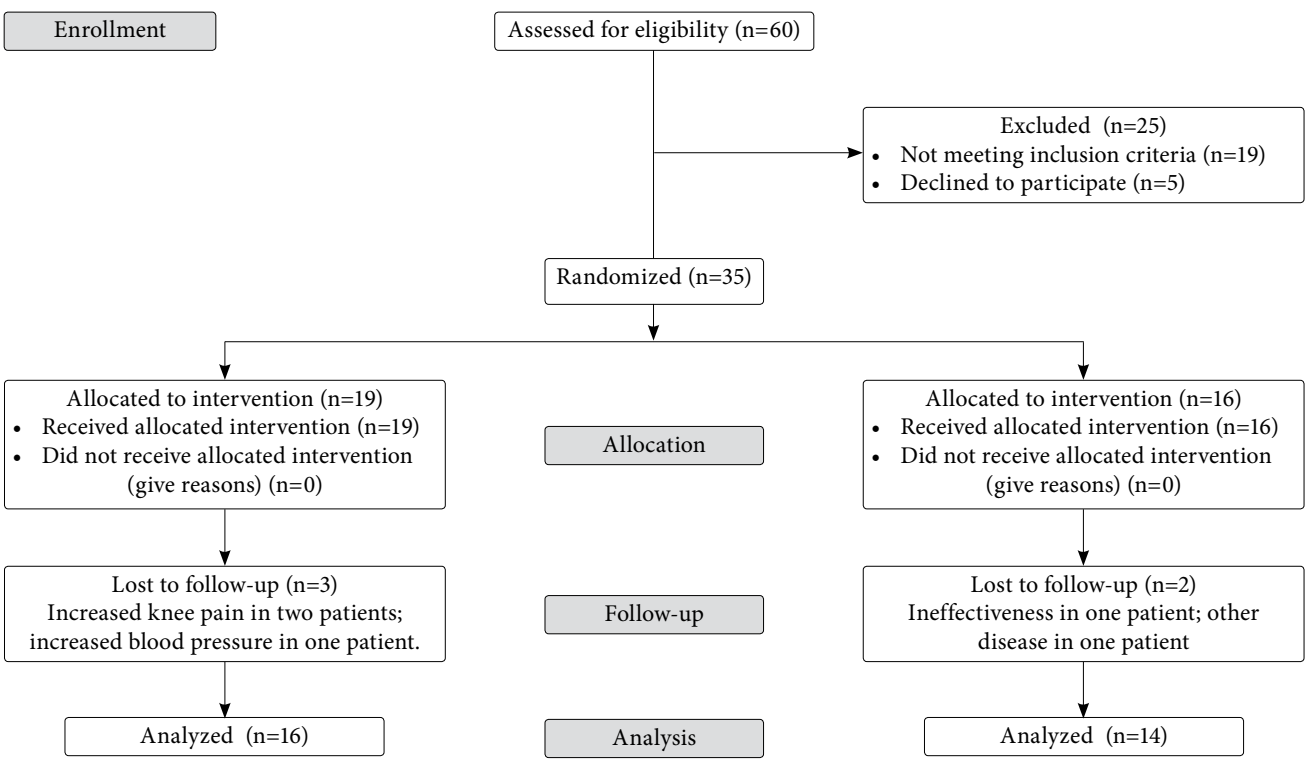

Figure 1. Patient flow chart.

response to exercise is not clear.[12-14] The use of magnetic resonance imaging (MRI) to examine the morphological characteristics of cartilage is a relatively new method. In addition to imaging, this study aimed to obtain objective data by measuring the thickness and the volume of the knee joint cartilage at various areas of the joint.

PATIENTS AND METHODS

Between December 2011 and May 2013, a total of 60 patients between 40 and 60 years of age who were referred to the Physical Medicine and Rehabilitation outpatient clinic were screened. Finally, 35 patients who were diagnosed with grade 1-3 OA in accordance with the American College of Rheumatology (ACR) criteria were enrolled.[15]

The exclusion criteria were as follows: systemic inflammatory arthritis, secondary knee OA and grade 4 OA, knee or hip replacement, diabetes mellitus, uncontrolled hypertension, respiratory disease, and cognitive or communicative impairments.

All physical examinations were performed by a single physician. The patients were randomly assigned into two groups as group 1 (exercise group, n=19) and group 2 (control group, n=16). The patient flowchart organized according to the Consolidated Standards of Reporting Trials (CONSORT) recommendations[16] are shown in Figure 1.

All patients were randomly assigned to the group 1 or group 2 using computer-generated numerical assignments. A sequence generator at random.org was used to create a random number sequence.[17] The sequence numbers was written in closed envelopes and each patient chose one to assign a group. The randomization procedure was implemented by a nurse.

The demographic data included the patient's age, sex, body mass index (kg/cm^2), and symptom durations.

The study protocol was approved by the Ethics Committee of the İstanbul University, Faculty of Medicine. A written informed consent was obtained from each patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Exercise program

Over a period of 15 days, the patients in the group 1 performed a 30 minute exercise regimen aimed at strengthening the quadriceps and hamstring muscles with the help of a physiotherapist in the first stage. Two physiotherapists were assigned to the intervention and both worked with the group 1 and group 2. Five treatment sessions were scheduled each week and the treatments were completed within 15 days. During the warm-up stage of the exercise session, the patients performed 10 repetitions of active knee extension (without any additional weight) while seating on an elevated table and 10 repetitions of active knee flexion while lying face down. After the warm-up period, each patient performed squat exercises with their own body weights. The patients leaned their backs against a sliding wall and placed their feet approximately a foot length forward. They were asked to slowly slide their body downward in this position with their hands free at their sides. When the knee flexion reached an angle of 60°, they were asked to stop and count to three in this position before returning to the starting position. The same movements were repeated after a 10 second break. This cycle was considered to be one set and each patient completed 15 sets. After 15 sessions with the physiotherapist, the patients continued the same regimen at home and they were called every two weeks to assess their adherence to the program. All patients were assessed with a checklist including the

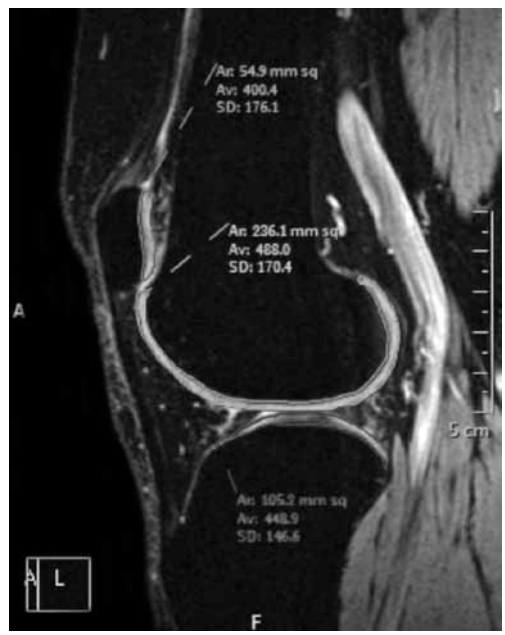

Figure 2. Heavily T_2-weighted spoiled gradient echo sequence with multiple echoes (3D MEDIC) in sagittal plane at the mid portion of knee joint. Measurements of patellar, femoral condyle and tibial plateau cartilage with the free hand region of interest method was seen.

method of squat exercises, number of repetitions, days off-exercise, and the presence of pain.

Electrotherapy and warm

The patients in group 1 and group 2 underwent hot-packet for 30 minutes along with transcutaneous electrical nerve stimulation (TENS) application. The TENS (ElettronicaPagany, S.R.L., Milano, Italy) program was selected from the pre-set list (pulse duration of 150 msec, frequency of 120 Hz, amplitude of 50 mA) and group 2 were not allowed to perform specific exercises beyond their daily life activities.

Magnetic resonance imaging acquisitions

Before and after interventions, the knees of all patients were examined with MRI using a 1.5-T System (Siemens Medical Solution, Erlangen, Germany) with a circumferential knee coil. A heavily T_2-weighted spoiled gradient echo sequence with multiple echoes (3D MEDIC; TR: 38, TE: 22, FOV: 160 mm, Slice Thickness: 0.7 mm, Flip angle: 7), fat-suppressed proton density (FS PD) in the axial, sagittal and coronal planes, and T_1-weighted sagittal images were applied. The data were transmitted to a Philips Brilliance Workstation for the volume assessment using the free hand region of interest (ROI) method.

A three-dimensional MEDIC sequence was used to calculate the femoral condyle, tibial plateau, and patellar cartilage volumes. We started with the free hand ROI calculation of the entire area of each cartilage moving from one part to another by 1.4 mm thick slices, until we observed the non-cartilaginous areas in the sagittal re-formatted plan. The sum of the total values was used to calculate the cartilage volume with the addition of the slice thickness.[18] Figure 2 shows the MRI evaluation variables and cartilage measurement methods.

The process for each patient was repeated separately by two different radiologists. The final volume was considered to be the mean of the calculated values. As automatic volume analysis software was not used, it took approximately one hour to measure the volume for each patient.

The patellar cartilage thickness was measured at the thickest region of the cartilage near the median tubercle of the patella in the axial PD sequence. Medial and lateral tibial plateau and femoral condyle cartilage thicknesses were measured using the coronal FS PD sequence through the mid portion of the joint, at which point the confirmation was performed with the sagittal cross-sectional images.[19]

Both radiologists were blinded to the patients' clinical data and interventions applied. We performed inter-rater reliability analysis for two radiologists to all MRI parameters. In this study, interclass correlation coefficient (ICC) values were between 0.718 and 0.953, except the medial femoral condyle with an ICC value of 0.654.

Pain and disability

Before starting the treatment, each patient completed a visual analog scale (VAS)-pain with a 100 mm horizontal line. The VAS is a valid and reliable measurement method to evaluate the pain. The measurements were quantified with a ruler and recorded. The severity of knee pain, stiffness, and functional condition were evaluated with a five-point Likert Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) v3.1, which is a valid, reliable and responsive measure of the outcome in knee and hip OA.[20] Both tests were performed before (week 0) and after (week 12) the treatment by a physiotherapist who was blinded to the patients.

Table 1. Baseline and demographic characteristics of the patient and control groups

	Group 1 (n=16)			Group 2 (n=14)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (years)			49.5±7.0			52.9±3.7	0.142
Sex							
Male	3	18.75		3	21.42		
Female	13	81.25		11	78.57		
Body mass index (kg/cm^2)			28.0±5.0			29.2±3.8	0.749
Symptom duration (months)			27.5±30.3			41.1±42.0	0.337
Visual analog scale (0-10 cm)			6.6±1.7			5.4±1.5	0.590
WOMAC-p (0-20)			9.9±4.1			11.1±4.3	0.464
WOMAC-s (0-8)			2.6±1.8			3.9±2.5	0.131
WOMAC-f (0-68)			24.5±14.0			27.7±11.0	0.523
WOMAC-t (0-96)			36.9±17.6			42.6±17.1	0.409

SD: Standard deviation; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Statistical analysis

We designed a study of a continuous response variable from matched pairs of the study population. Prior data indicate that the difference in the response of matched pairs is normally distributed with a standard deviation of 0.6. If the true difference in the mean response of matched pairs is 0.4, we need to study 20 pairs of subjects to be able to reject the null hypothesis that this response difference is zero with a probability of 0.8 (study power). The type 1 error probability associated with this test of this null hypothesis is 0.05.

Statistical analyses were performed using the IBM SPSS for Windows version 20.0 software (IBM Corporation, Armonk, NY, USA). Since the intra-group comparisons did not exhibit a normal distribution, non-parametric tests were used. The Wilcoxon test was used to analyze a significant relationship between pre- and post-treatment values. The Mann-Whitney U t test was used to detect significance between the groups (for both pre- and post-treatment values). A p value of <0.05 was considered statistically significant.

RESULTS

The baseline data and demographic characteristics of group 1 and group 2 are described in Table 1. There were no significant differences in age (years), body mass index (kg/cm^2), symptom duration (months), pain intensity (VAS) scores, and WOMAC-total and WOMAC-subtest scores between the two groups (p>0.05).

In group 1, there was only a significant difference in the tibial cartilage volume between the pre- and post-treatment values (p<0.05). There were no significant differences in other volumetric and thickness measurements (p>0.05). On the other hand, group 2 did not show any significant differences in terms of pre- and post-treatment values (p>0.05). The groups were compared after the cartilage volume was treated and there were no significant differences in the post-treatment cartilage volume and thickness measurements between the groups. Table 2 shows the baseline and post-treatment cartilage MRI data.

In addition, the intragroup comparisons revealed significant differences in the pre- and post-treatment values of the VAS, WOMAC-pain, WOMAC-physical

Table 2. Pre- and post-treatment results of cartilage based on magnetic resonance imaging findings

	Group 1 (n=16)			Group 2 (n=14)			Post-treatment values of group 1 vs. group 2
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment		
	Mean±SD	Mean±SD	p	Mean±SD	Mean±SD	p	p
Total cartilage volume (mm^3)	4594.7±4406.4	4866.8±5005.8	0.055	5026.8±2313.7	4999.1±2215.5	0.445	0.236
Patellar cartilage volume (mm^3)	832.4±482.2	890.8±699.6	0.780	929.2±445.5	881.3±437.8	0.168	0.649
Tibial cartilage volume (mm^3)	1437.2±920.4	1528.8±931.1	0.001	1205.5±438.9	1184.4±391.2	0.424	0.494
Femoral cartilage volume (mm^3)	3284.8±3102.7	3462.3±3507.7	0.071	3349.1±1158.7	3387.9±1115.9	0.213	0.091
Medial femoral condyle thickness (mm)	2.6±0.7	2.6±0.7	0.932	2.3±0.8	2.3±0.8	0.960	0.695
Lateral femoral condyle thickness (mm)	2.5±0.6	2.5±0.6	0.726	2.3±0.6	2.3±0.6	1.00	0.487
Medial tibial plateau thickness (mm)	2.1±0.5	2.1±0.4	0.450	2.0±0.5	2.1±0.5	0.271	0.651
Lateral tibial plateau thickness (mm)	2.3±0.6	2.4±0.6	0.161	2.1±0.6	2.1±0.5	0.257	0.413
Patellar cartilage thickness (mm)	3.3±0.9	3.3±0.8	0.596	3.6±0.9	3.6±1.0	0.339	0.649
Trochlear cartilage thickness (mm)	2.9±0.9	2.9±1.0	0.958	3.0±0.9	3.0±0.9	0.748	0.928

SD: Standard deviation; p<0.05 significant; 95% CI: 95% Confidence interval.

Table 3. Pre- and post-treatment results of visual analog scale, Western Ontario and McMaster Universities Osteoarthritis Index, pain, stiffness and physical function domains

	Group 1			Group 2			Post-treatment values of group 1 vs. group 2
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment		Pre-treatment
	Mean±SD	Mean±SD	*p*	Mean±SD	Mean±SD	*p*	*p*
VAS (0-10 cm)	6.6±1.7	1.7±0.9	0.001	5.7±1.5	3.6±2.8	0.016	0.075
WOMAC-pain (0-20)	9.9±4.1	3.2±1.9	0.001	11.1±4.3	7.2±5.1	0.001	0.053
WOMAC-morning stiffness (0-8)	2.6±1.8	1.1±1.2	0.009	3.9±2.5	1.8±2.1	0.004	0.614
WOMAC- physical function (0-68)	24.5±14.0	6.7±3.7	0.001	27.7±11.0	19.8±13.8	0.036	0.004
WOMAC-total (0-96 point)	36.9±17.6	13.5±9.8	0.001	42.6±17.1	29.0±19.6	0.010	0.025

SD: Standard deviation; VAS: Visual analog scale, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; p<0.05 significant; 95% CI: 95% Confidence interval.

function, and WOMAC-stiffness scores between group 1 and group 2 (p<0.05). In the intergroup analysis, we also founded significant differences for all post-treatment VAS and WOMAC scores, except for WOMAC-stiffness (p<0.05) (Table 3).

DISCUSSION

The primary goal of this study is as to evaluate the extent to which cyclical loading on the knee joint affects the cartilage synthesis and repair processes, and the secondary goal is to evaluate the positive impact of exercise on pain and physical function. In this study, we showed that closed kinetic chain exercise was ineffective on the knee cartilage volume and thickness. However, we do not have sufficient information to indicate that articular cartilage network and GAG matrix affected from the MRI studies. On the other hand, the high magnetic field may have led to some changes in the micro-architecture. Additionally, our study repeatedly confirmed the positive effects of exercise on pain and functionality.

The major structural change in the OA physiopathology is the loss of cartilage. Damage to collagen fibers due to mechanical or inflammatory processes leads to aggrecan decomposition, causing fiber oversaturation with water and mechanical loading-induced degeneration.[21] It is usually considered that continuous and excessive loads are destructive to the cartilage, whereas cyclical and reasonable loadings are thought to be beneficial.[22,23]

Roos and Dahlberg.[12] tested how cyclical loading-based mild exercise repeated three times a week changed the GAG content of the cartilage in a randomized controlled follow-up study. The primary goal of this study was to show the change in the GAG content in the cartilage matrix. The authors concluded that the exercise regimen performed for four months led to a meaningful increase in the GAG content compared to the control group.[12] Although the authors did not measure the cartilage volume, the study is important, as it demonstrated increased the GAG content which is an important building block of cartilage health and morphology. Thus, these results are not similar to our findings, as Roos and Dahlberg's[12] findings indirectly demonstrated that exercise increased the production of cartilage. In contrast to the findings of Roos and Dahlberg,[12] Multanen et al.[14] showed that progressively implemented high-impact training did not affect the biochemical composition of the cartilage. In another study, Durmus et al.[13] detected an increased cartilage volume and thickness in both groups, when they evaluated the impacts of aerobic exercise combined with glucosamine on the knee joint cartilage; however, they did not observe any inter-group differences between the two groups. While the results of our study are similar to the findings reported by Durmus et al.[13] in terms of pain and WOMAC-physical function domains, the cartilage variables differed considerably.

In an observational study of 297 healthy individuals, Racunica et al.[24] examined the impact of strong physical activity. After monitoring regular activity for four years, they found a meaningful increase in the tibial cartilage section. Their study evaluated on healthy individuals and its primary goal was not to test healing in the cartilage. However, it clearly demonstrates the protective effect of cartilage against OA and bone marrow edema. On the other hand, the results of the aforementioned study were not similar to our results. We treated exercise group with closed kinetic chain exercises which provided loading

on the joint cartilage for a period of three months and we observed an increase in the tibial cartilage volume in the exercise group only. However, the aforementioned authors reported that weight-bearing vigorous activity increased with tibial cartilage volume after treatment. In another study, Racunica et al.[24] enrolled only healthy adults (i.e., free of knee injury or disease) and only measured tibial cartilage volume. However, we studied patients with grade 1-3 OA and measured all cartilage variables. These results suggested that the response to exercise might differ osteoarthritic and healthy cartilage. The increased in cartilage volume is explained by chondrocyte proliferation, increased expression of cartilage aggrecans, Type 2 collagen and matrix macromolecules through hydrostatic pressure.[25,26] However, it is unknown whether unhealthy cartilage produces the same response to the exercise.

Cotofana et al.[27] performed a longitudinal study which examined the impacts of endurance and strengthening exercises on the joint cartilage in healthy middle-aged woman. At three month, they did not observe a significant difference in the cartilage volume or cartilage thickness between the treatment and control groups. The authors concluded that exercises performed for three months did not lead to significant changes within the groups, either. To a great extent, these results are consistent with our findings, as we did not observe significant differences between the exercise and control groups at the end of the study, either. These results also support the view that exercise does not increase the cartilage volume. In a rat model, Dong at al.[28] found that both low- and moderate-intensity exercises failed to promote re-surfacing of the full-thickness cartilage defects on the patellofemoral articular surface and high-intensity exercise even induced subchondral bone damage. However, Foley et al.[29] examined the impact of lower extremity muscular strength and exercise capacity on the tibial plateau area and cartilage volume. The authors demonstrated that endurance exercise might prevent loss of cartilage tissue in women, particularly. Kersting et al.[30] examined the changes which occurred in the cartilage in runners. They concluded that co-activation of the flexor and extensor muscles was the underlying force behind the increased cartilage volume. Similarly, Boocock al.[31] showed that running for short periods increased the cartilage volume. We believe that the increased cartilage volume demonstrated by both studies was caused by an accumulation of water resulting from high-frequency loading-induced elastic deformation. Our study had a relatively longer monitoring period and we did not collect images immediately after the exercises. Therefore, our study can depict the response of the joint cartilage to exercise with a greater accuracy. Loyola-Sánchez et al.[32] also reported an increased medial tibial cartilage in OA patients during 25 ultrasound sessions. However, the results of this study contradict with our findings and can be attributed to different healing variables (i.e., cartilage thickness, subchondral cysts, and subchondral bone thickness).

Furthermore, many studies have shown that exercise improves patellofemoral pain.[33] In our study, the mean VAS scores for the treatment group who regularly performed squat exercises, were significantly lower than the baseline values. Similarly, the treatment group was significantly differed from the controls in terms of the WOMAC-pain and WOMAC-physical function domains. Although squat exercises did not lead to a significant increase in the cartilage volume and thickness, improvement in pain and physical function domains may have been due to an increased peri-articular muscle mass. Durmus et al.[13] also observed increased muscle strength values in the exercise group and these results support the argument that muscular performance alleviates pain. Despite the studies which showed the positive impact of muscular activity of the lower extremity on the joint cartilage volume,[29] whether joint cartilage in adults have phenotypic plasticity and how respond to exercise is not definitely known, yet.[34,35] Moreover, although exercise significantly improves OA symptoms, the impact of exercise on the structural characteristics of the cartilage in joints with OA is still unclear. Additionally, aerobic exercises for an appropriate intensity and duration can cause both an increased endorphin secretion and normalization in the gait control mechanism.[36,37] Squat exercises prevent patellar lateralization and improve alignment, thereby, decreasing pain and improving the functional level.[38] These mechanisms also explain why the exercise group had lower VAS and WOMAC scores in our study.

However, there are some limitations to our study. First, our sample size was relatively small and the follow-up period was relatively short. Since there was no clear information on the cartilage turnover speed and periodicity, it is unknown at what point the cartilage optimally responds to exercise. Therefore, we were unable to explain how the volume and thickness of cartilage in patients changed in subsequent periods. Second, the degree of adherence to the home exercises of the patients is unknown.

Additionally, for ethical reasons, the patients in the control group were not prevented from performing walking exercises, which can be considered to be a type of closed kinetic chain exercises. Third, the exercises were performed with each patients' own body weights, which prevented the use of standard loading on the joint cartilage. Fourth, in our study, three subjects in the exercise group and two subjects in the control group were withdrawn. In such cases, the CONSORT guideline proposes an intention-to-treat analysis. However, we were unable to perform repeated measurements in this process. We have only baseline data of these subjects, which hindered an intention-to-treat analysis. Fifth, we used a 1.5 Tesla MRI device. The sensitivity of this device is lower than lower than 3 Tesla MRI in detection of small cartilage changes, in particular. Additionally, relatively low ICC may be difficult to show the effects of closed kinetic chain exercise. Finally, we did not reach the target number of patients due to the patients who withdrew from the study.

In conclusion, based on our study results, we showed no significant effect of closed kinetic chain exercise on the cartilage volume or morphology during follow-up. Reduced pain can be attributed to the possible changes in the biochemical composition of the cartilage and synovium. However, further long-term studies are required to establish a definite conclusion.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

This study was financially supported by the Haydarpasa Training Hospital Research (2012- Project no: 121).

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