



# Effects of isokinetic, isometric, and aerobic exercises on clinical variables and knee cartilage volume using magnetic resonance imaging in patients with osteoarthritis

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Received: September 2016 Accepted: February 2017

## ABSTRACT

**Objectives:** This study aims to evaluate the effect of isokinetic, isometric, and aerobic exercise protocols on pain, disability, physical function, and articular cartilage in osteoarthritis.

**Patients and methods:** A total of 45 women (mean age 52.1 years; range 45 to 65 years) who were admitted to the Physical Medicine and Rehabilitation outpatient clinic and were diagnosed with primary bilateral knee osteoarthritis between May 2008 and January 2010 were included. The patients were randomly divided into three groups as isokinetic (n=15), aerobic (n=15), and isometric exercise groups (n=15). Exercise protocols were applied five days a week for four weeks. Pain was evaluated using a 10 cm Visual Analog Scale for Pain (VAS-pain), pain, joint stiffness and physical function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), and disability was assessed using the Lequesne Index before and after the interventions. Isokinetic knee muscle strength measurements were also obtained. Patellar and femoral cartilage volumes were analyzed using magnetic resonance imaging.

**Results:** The VAS-pain, WOMAC, and Lequesne scores and peak torque values of knee extension improved in all groups with the highest improvement in the isokinetic group. For the knee flexion peak torque values, improvements were significant only in the isokinetic group at both velocities. There was no significant change in the femoral cartilage volume in any group after the interventions. However, patellar cartilage volume significantly increased in the isometric group (p=0.036).

**Conclusion:** A four-week isokinetic, aerobic, and isometric exercise programs improved pain and functional capacity in patients with knee osteoarthritis. Isokinetic exercise also increased the muscle strength with improved maintenance of the quadriceps/hamstring ratio. Only isometric exercise increased the patellar cartilage volume.

**Keywords:** Cartilage; exercise; knee osteoarthritis; magnetic resonance imaging.

Osteoarthritis (OA) is a common form of arthritis characterized by loss of articular cartilage.<sup>[1]</sup> It is one of the major causes of physical disability and is the most common indication for hip and knee replacement.<sup>[2]</sup> The main symptoms of OA are pain and loss of function.<sup>[3]</sup>

Exercise is a non-pharmacological treatment modality recommended in the guidelines of the management of knee OA.<sup>[3-5]</sup> Although exercise reduces pain, improves physical function, aerobic capacity and endurance, and helps in weight reduction, there are

still ongoing debates about the effects of exercise on the articular cartilage.<sup>[6,7]</sup> Exercise may have a direct effect on the articular cartilage and an indirect effect through actions on muscles. Muscles play a key role in maintaining the normal biomechanics of the joint. Strengthening the quadriceps and hamstring muscles improves the joint stability. It has been shown that mechanical stimulation increases the biosynthetic activity of chondrocytes, and thickness of the cartilage adapts to mechanical loading in animal models.<sup>[8]</sup> On the other hand, intense physical activity may increase the risk of OA.<sup>[9,10]</sup>

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Cite this article as:

Benli Küçük E, Özyemişçi Taşkıran Ö, Tokgöz N, Meray J. Effects of isokinetic, isometric, and aerobic exercises on clinical variables and knee cartilage volume using magnetic resonance imaging in patients with osteoarthritis. Turk J Phys Med Rehab 2018;64(1):8-16.

Magnetic resonance imaging (MRI) has enabled a direct evaluation of the articular cartilage. Using MRI, it is possible to assess the macro-morphological properties of the cartilage, i.e., thickness, surface area and volume of the articular cartilage. Surface irregularities of the cartilage and other structural changes in the joint can be also evaluated.<sup>[11]</sup> Magnetic resonance imaging has multi-planar imaging capability, high spatial resolution without ionizing radiation, and superior contrast between the tissues of the joint.<sup>[12]</sup> Therefore, it has gained popularity in the assessment of OA and the effects of exercise on the cartilage in recent years.

There are numerous studies investigating short-term effects of exercise on the cartilage.<sup>[13-18]</sup> Deformation of the articular cartilage occurs shortly after exercise or physical activity<sup>[2]</sup> and it takes about 90 min to recover after loading.<sup>[13]</sup> During daily activities, patellar cartilage is subjected to 2 to 3% compression, compared to non-weight-bearing states.<sup>[13]</sup> Vigorous exercise adds another 2 to 3% compression over that of daily activities.<sup>[13]</sup> Previously, deformation has been shown to be more prominent in the patellar cartilage, compared to the femoral and tibial cartilage.<sup>[13-17]</sup>

In the literature, studies addressing into the long-term effects of exercise on the cartilage are mostly cross-sectional,<sup>[11,19,20]</sup> while the number of longitudinal studies has been also increasing in recent years.<sup>[21-23]</sup> These studies, which primarily include healthy individuals without knee pain, have demonstrated that intense physical activity has beneficial effects on the articular cartilage of the knee<sup>[11,21]</sup> and reduces cartilage loss in healthy adults.<sup>[22,23]</sup> However, studies comparing the cartilage morphology of physically inactive subjects with that of athletes have shown that deformational behavior of the cartilage in the short-term after exercise is similar.<sup>[15,17]</sup> In the long-term, the cartilage thickness is not different between athletes and physically inactive subjects,<sup>[19,20]</sup> except for the study of Grtazke et al.<sup>[20]</sup> who reported that only patellar cartilage was thicker in athletes.

In another study, Teichtahl et al.<sup>[23]</sup> recruited healthy adults without clinical knee disease and found no relationship between vigorous physical activity and cartilage volume change or defect progression in the subgroup with prevalent patellar cartilage defects at baseline. However, the effects of exercise on the morphological features of articular cartilage in patients with knee OA have not been investigated using MRI, yet.

In the present study, we hypothesized that isokinetic and aerobic exercises would increase the muscle strength at the expense of reduction in the cartilage volume and both effects would be stronger after isokinetic exercises. Our second hypothesis was that isometric exercise would not alter the isokinetic muscle strength or cartilage morphology, but would reduce symptoms and increase the functional capacity. Therefore, we aimed to investigate the effects of isokinetic, isometric, and aerobic exercise protocols on the pain, functional capacity, muscle strength, and knee cartilage using MRI in patients with knee OA.

## PATIENTS AND METHODS

This prospective, comparative study was approved by the Research Ethics Committee of Medical Faculty, Gazi University and conducted in accordance with the principles of the Declaration of Helsinki. A verbal and written informed consent was obtained from each participant.

A total of 45 women (mean age 52.1 years; range 45 to 65 years) who were admitted to the Physical Medicine and Rehabilitation outpatient clinic at a tertiary setting and were diagnosed with primary bilateral knee osteoarthritis according to the American College of Rheumatology criteria<sup>[24]</sup> between May 2008 and January 2010 were included. All patients had radiological Grade 2 or 3 diseases, according to the Kellgren-Lawrence scale and were able to follow the exercise instructions. Patients with severe cardiac and pulmonary diseases, uncontrolled hypertension, inflammatory joint disease, prominent joint instability, previous knee surgery, lower extremity pathology other than knee OA, and those with an MRI contraindication were excluded from the study.

Eligible patients were randomly divided into three groups as isokinetic (n=15), aerobic (n=15), and isometric exercise groups (n=15). A detailed history and physical examination findings including deformity, range of motion, swelling, tenderness, patellar mobility, crepitation, and ligament laxity in the knee joints were recorded. Age, height, weight, and body mass index were also noted.

Before and after interventions, self-reported pain severity during daily activities (i.e., walking, climbing stairs, and resting at night) was measured using the 10 cm Visual Analog Scale for Pain (VAS-pain). The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) was used to evaluate

pain, joint stiffness, and physical function.<sup>[25]</sup> The Lequesne Index was used to assess disability.

The knee flexion and extension strength measurements were performed using the Cybex 770 Norm (Lumex Inc, Rankokoma, NY, USA) isokinetic dynamometer before and after the interventions. All measurements were performed, while the patient was seated with hip and knee joints flexed at 90° and chest, trunk, and thigh proximal to the knee joint stabilized by straps. The lever arm was adjusted for the leg length of the patient and secured with a strap proximal to the ankle. The weight of the tested leg was measured before the test and the effect of gravity was adjusted by the dynamometer. Full extension of the knee joint was considered anatomical zero position. Tests were performed in a subject-specific range of motions, which were measured by the dynamometer. All measurements were performed before and after the interventions. Reciprocal concentric knee flexion and extension were evaluated at two angular velocities; 60°/sec and 180°/sec. Before testing, the patient was instructed about the each test and, with each angular velocity, four submaximal contractions were performed by the patient to become familiar with the tests. After the practice, the patient relaxed for a period of 10 sec before test trials. During the measurements at 60°/sec angular velocity, the patient was asked to perform five repetitions of flexion and extension as forcefully as possible. Measurements at 180°/sec angular velocity were performed after resting for 20 sec. This time participants were asked to perform 20 repetitions of flexion and extension as soon as possible. The patient was, then, allowed to rest for 5 min between the measurements of the right and left knee. The peak torque values of the right knee recorded in foot-pounds (FtLbs) using the HUMAC software version 8.2.1 (Computer Sports Medicine, Inc., Stoughton, MA, USA) were used in the data analysis.

### **Interventions**

All patients were instructed not to use non-steroidal anti-inflammatory drugs during the study period. Only paracetamol was allowed, if needed, as an escape analgesic; however, it was not allowed to take paracetamol 24 hours before the assessment. Each participant performed the exercise protocols relevant to their group five days a week for four weeks in the orthopedic rehabilitation unit under the supervision of a research physiatrist (E.B.K.). All patients completed the exercise program relevant to their group and no patient was withdrawn from the study.

In the isokinetic group, the patients performed exercise using Cybex Norm Model 770 isokinetic dynamometer (Cybex, division of Lumex Inc., Ronkonkoma, NY, USA). After warming up, they performed 10 concentric-concentric flexion and extension contractions at 60°, 90°, 120°, 150° and 180°/sec angular velocity with 20 sec rests rest between each angular velocity and five-min rest between the right and left knees. In the isometric group, the patients performed 10 straight leg raise and 10 quadriceps isometric contractions holding for 10 sec with knee 90° flexion and knee 180° extension and a 2 min rest period between. In the aerobic group, the patients walked at 4.5 km/hour velocity on a treadmill for 20 min.

After the interventions, transcutaneous electrical stimulation (TENS) and cold pack were applied to both knees of all patients in the three intervention groups for 20 min.

A 1.5 Tesla MRI unit (Signa, Excite II, General Electric Medical Systems, Milwaukee, Wisconsin, USA) was used to assess the knee cartilage. Imaging of the knee was performed using a knee coil in the sagittal plane. A T-weighted fat-saturated spoiled gradient recalled acquisition in the steady state (SPGR) imaging sequence was performed in the sagittal plane using the following parameters: TR 40 ms; TE 7 ms; flip angle 40°; field of view 18×15 cm; matrix 288×224; number of excitations 2; slice thickness 1.5 mm, inter-slice gap zero.

An independent workstation was used for the image analysis. During the analysis of MRI images, femoral and patellar articular cartilages were outlined manually using electronic cursors on a slice by slice basis. The volumes of the cartilages were derived automatically using commercially available software (Advantage Workstation, release 4.1, GE Healthcare, Waukesha, Wisconsin, USA). An experienced musculoskeletal radiologist performed the measurements on images within two days. To assess the intra- and inter-observer variations, the images of 15 patients were re-measured by the same observer and another radiologist in the following week.

The intra-class correlation coefficient (ICC) was used to evaluate the intra- and inter-observer correlations in two measurement sessions. The ICC indicated a high intra- and inter-observer reliability, as the value ranged from 0.83 to 0.91 for all measurements.

### **Statistical analysis**

Statistical analysis was performed using the SPSS for Windows version 15.0 (SPSS Inc., Chicago, IL, USA).

**Table 1.** Demographic and clinical characteristics of the participants

|   | Isokinetic group (n=15) |    |           | Aerobic group (n=15) |    |           | Isometric group (n=15) |    |           | <i>p</i> |
|---|-------------------------|----|-----------|----------------------|----|-----------|------------------------|----|-----------|----------|
|   | n                       | %  | Mean±SD   | n                    | %  | Mean±SD   | n                      | %  | Mean±SD   |          |
| Age (year)  |                         |    | 51.5±5.0  |                      |    | 52.5±5.3  |                        |    | 52.3±6.9  | 0.863    |
| Body weight (kg)  |                         |    | 74.9±12.8 |                      |    | 74.1±12.6 |                        |    | 71.9±14.8 | 0.762    |
| Body height (cm)  |                         |    | 157.7±4.5 |                      |    | 157.7±7.8 |                        |    | 155.6±7.5 | 0.768    |
| Body mass index (kg/cm <sup>2</sup> )                   |                         |    | 30.1±5.0  |                      |    | 29.6±3.5  |                        |    | 29.9±7.2  | 0.980    |
| Radiographic Grade of right knee<br>(Kellgren-Lawrence) |                         |    |           |                      |    |           |                        |    |           | 0.435    |
| Grade 2   | 8                       | 53 |           | 11                   | 73 |           | 8                      | 53 |           |          |
| Grade 3   | 7                       | 47 |           | 4                    | 27 |           | 7                      | 47 |           |          |

SD: Standard deviation.

The Shapiro-Wilk test was used to test the normality of distribution of each of the variable. Categorical variables were expressed in median and/or mean ± standard deviation (SD) for quantitative variables and proportions (%). The Kruskal-Wallis test was used to test the significant differences in age, weight, height, body mass index, and also the baseline measurements of VAS, WOMAC scores, Lequesne Index, peak torque measurements and femoral and patellar cartilage volumes among the groups. The Wilcoxon signed-rank test was used to compare pre- and post-exercise values within the same group for VAS, WOMAC scores, Lequesne Index, peak torque measurements and femoral and patellar cartilage volumes. Two-way mixed analysis of variance (ANOVA) was used to compare the effect of exercise programs on VAS, WOMAC scores, Lequesne Index, peak torque measurements, and femoral and patellar cartilage volumes among the groups. The chi-square

test was used to compare the radiographic Grades of the right knee (Kellgren-Lawrence) among the groups. A *p* value of <0.05 was considered statistically significant.

## RESULTS

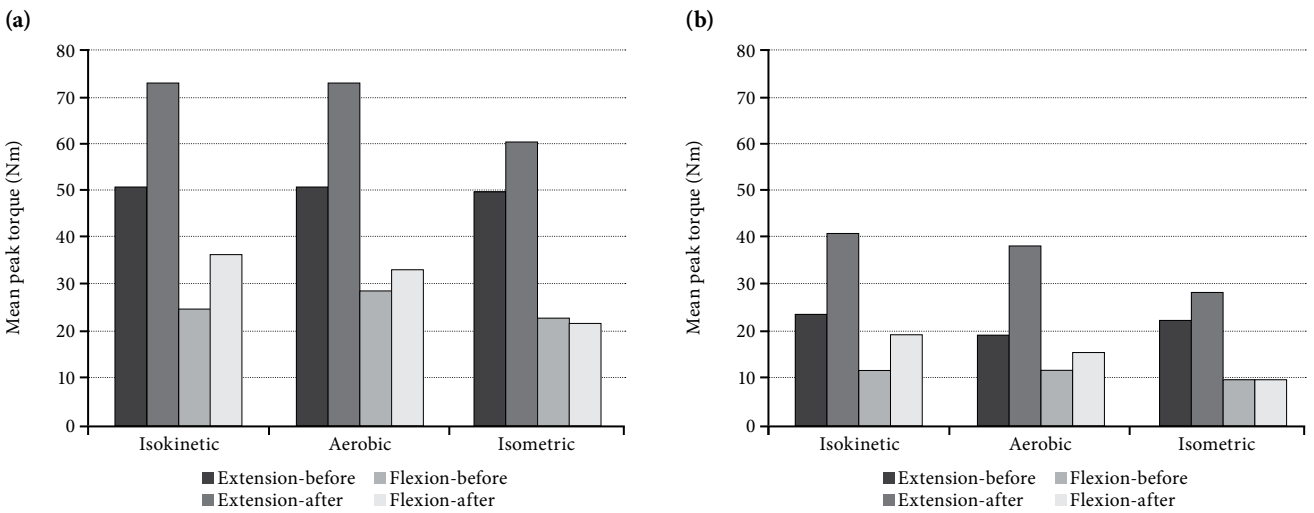
Forty-five women with bilateral knee OA completed the study. There were no significant differences in age, weight, height, body mass index among the groups. Although a higher proportion of patients in the aerobic group was Grade 2 according to the Kellgren-Lawrence grading scale, this difference was not statistically significant among the exercise groups (*p*=0.435) (Table 1).

Baseline values of outcome parameters are presented in Table 2. There were no significant differences in the VAS-scores during the night, climbing stairs or walking; WOMAC subscores of pain, stiffness and

**Table 2.** Pain scores according to VAS, WOMAC, and Lequesne Index before and after interventions

|                   | Isokinetic group (n=15) |             | Aerobic group (n=15) |             | Isometric group (n=15) |             | <i>p</i> |
|-------------------|-------------------------|-------------|----------------------|-------------|------------------------|-------------|----------|
|                   | Median                  | Min-Max     | Median               | Min-Max     | Median                 | Min-Max     |          |
| VAS-walking (cm)  | 7.0                     | 4.0-9.0     | 7.0                  | 5.0-9.0     | 7.0                    | 5.0-9.0     | 0.776    |
|                   | 4.0                     | 2.0-9.0**   | 4.0                  | 2.0-6.0**   | 4.0                    | 2.0-5.0**   |          |
| VAS-night (cm)    | 5.0                     | 1.0-8.0     | 2.0                  | 1.0-7.0     | 4.0                    | 1.0-7.0     | 0.781    |
|                   | 2.0                     | 1.0-4.0**   | 2.0                  | 1.0-5.0*    | 2.0                    | 1.0-4.0**   |          |
| VAS-climbing (cm) | 8.0                     | 6.0-10.0    | 7.0                  | 5.0-9.0     | 7.0                    | 6.0-9.0     | 0.956    |
|                   | 4.0                     | 2.0-8.0**   | 5.0                  | 4.0-6.0**   | 4.0                    | 3.0-6.0**   |          |
| WOMAC-pain        | 14.0                    | 11.0-20.0   | 15.0                 | 10.0-19.0   | 15.0                   | 9.0-19.0    | 0.933    |
|                   | 8.0                     | 5.0-18.0**  | 8.0                  | 7.0-12.0**  | 7.0                    | 5.0-12.0**  |          |
| WOMAC-stiffness   | 5.0                     | 2.0-8.0     | 6.0                  | 2.0-8.0     | 6.0                    | 2.0-8.0     | 0.490    |
|                   | 3.0                     | 2.0-8.0*    | 3.0                  | 2.0-6.0**   | 4.0                    | 2.0-6.0**   |          |
| WOMAC-function    | 43.0                    | 32.0-60.0   | 45.0                 | 34.0-71.0   | 48.0                   | 28.0-66.0   | 0.990    |
|                   | 25.0                    | 20.0-68.0** | 25.0                 | 21.0-47.0** | 30.0                   | 20.0-38.0** |          |
| WOMAC-total       | 62.0                    | 50.0-83.0   | 63.0                 | 50.0-96.0   | 72.0                   | 39.0-92.0   | 0.975    |
|                   | 37.0                    | 28.0-94.0** | 35.0                 | 31.0-65.0** | 42.0                   | 27.0-50.0** |          |
| Lequesne Index    | 11.0                    | 7.0-18.0    | 11.0                 | 6.0-15.0    | 10.0                   | 6.0-15.0    | 0.519    |
|                   | 6.0                     | 1.0-13.0**  | 6.0                  | 3.0-11.0**  | 5.0                    | 3.0-8.0**   |          |

VAS: Visual Analog Scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; Min: Minimum; Max: Maximum; \* *p*≤0.05; \*\* *p*≤0.01; difference after intervention within the same group; The results before the interventions are depicted in the first line and the results after the interventions are depicted in the second line. *P* values are defined for the comparison of differences (before and after interventions) among the groups.



**Figure 1.** Peak torque measurements of the right knee flexion and extension at (a) 60°/sec and (b) 180°/sec angular velocity before and after interventions among groups.

function or total scores; Lequesne disability scores; peak torque values of knee flexion or extension measured at 60° and 180°/sec angular velocities; patellar or femoral cartilage volumes before the interventions among the three groups.

Significant improvements in pain scores during daily activities (i.e., walking, climbing up and down stairs, and night pain) were observed in all groups after the interventions, although the difference did not reach statistical significance (Table 2).

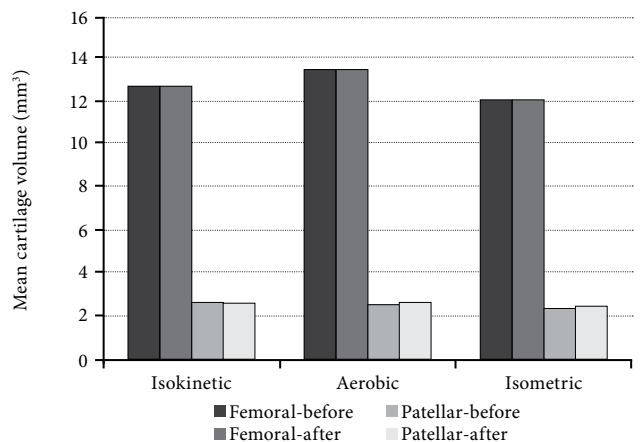
The peak torque values of the knee flexion and extension measured at 60° and 180°/sec angular velocities of the right knees in all groups are shown in Figure 1a, b. In the isokinetic group, the peak torque values of the knee flexion and extension at 60° and 180°/sec angular velocities improved significantly after four-week training ( $p=0.003$  and  $p=0.007$  for 60°/sec;  $p=0.009$  and  $p=0.004$  for 180°/sec, respectively). In the aerobic group, the peak torque improvements in knee extension were statistically significant ( $p=0.008$  for 60°/sec;  $p=0.009$  for 180°/sec), whereas those of the knee flexion were not ( $p=0.293$  and  $p=0.148$ ). In the isometric group, the peak torques of knee extension at both velocities increased significantly ( $p=0.025$  for 60°/sec;  $p=0.041$  for 180°/sec). However, the flexion peak torques did not change significantly ( $p=0.683$  and  $p=0.864$ ).

The improvements in the knee flexion peak torque at 60°/sec angular velocity were not significantly different among groups ( $p=0.094$ ). Also, the improvements in knee flexion peak torque at 180°/sec angular velocity did not reach statistical significance

( $p=0.071$ ). The changes in the peak torques were not different significantly for knee extension at 60°/sec or 180°/sec angular velocities ( $p=0.522$  and  $p=0.344$ , respectively) among the groups.

The hamstring/quadriceps ratio remained nearly unchanged in the isokinetic group and decreased in the aerobic and isometric groups ( $p=0.172$  and  $p=0.017$ , respectively); however, only this ratio was significant in the isometric group.

The femoral and cartilage volumes of right knees before and after the interventions are shown in Figure 2. No significant change in femoral cartilage volume was observed in any of the groups after the interventions (Figure 2, Table 3). Regarding patellar cartilage volume, the mean difference was found



**Figure 2.** Femoral and patellar cartilage volumes before and after interventions.

**Table 3.** Femoral and patellar cartilage volumes before and after interventions

|                     | Femoral cartilage (mm <sup>3</sup> ) |        |             |                |        |             | Patellar cartilage (mm <sup>3</sup> ) |         |         |                |         |         |           |       |
|---------------------|--------------------------------------|--------|-------------|----------------|--------|-------------|---------------------------------------|---------|---------|----------------|---------|---------|-----------|-------|
|                     | Before exercise                      |        |             | After exercise |        |             | Before exercise                       |         |         | After exercise |         |         |           |       |
|                     | Mean±SD                              | Median | Min-Max     | Mean±SD        | Median | Min-Max     | Mean±SD                               | Median  | Min-Max | Mean±SD        | Median  | Min-Max | p*        |       |
| Isokinetic exercise | 12.6±1.8                             | 12.35  | 10.10-15.90 | 12.6±1.9       | 12.58  | 9.37-15.99  | 0.657                                 | 2.6±0.5 | 2.44    | 2.11-3.32      | 2.5±0.5 | 2.58    | 1.62-3.41 | 0.533 |
| Aerobic exercise    | 13.4±1.4                             | 13.41  | 11.75-15.32 | 13.6±1.4       | 13.90  | 11.60-15.28 | 0.401                                 | 2.6±0.4 | 2.42    | 2.13-3.32      | 2.6±0.4 | 2.56    | 2.04-3.43 | 0.327 |
| Isometric exercise  | 12.0±1.7                             | 12.53  | 9.87-14.31  | 12.0±1.7       | 12.69  | 9.77-13.98  | 1                                     | 2.2±0.3 | 2.17    | 1.99-2.90      | 2.4±0.3 | 2.28    | 1.93-3.05 | 0.036 |
| p†                  |                                      |        |             |                |        |             |                                       |         |         |                |         |         |           | 0.338 |

SD: Standard deviation; Min: Minimum; Max: Maximum; p\*: Difference after intervention within the same group (Wilcoxon signed-rank test); p†: Between groups comparison (Two-way mixed ANOVA).

to be statistically significant in the isometric group ( $2.24\pm 0.29$  and  $2.35\pm 0.34$  mm<sup>3</sup> before and after intervention, respectively,  $p=0.036$ ), whereas in the isokinetic and aerobic groups the changes did not significantly differ ( $p=0.533$  and  $p=0.327$ , respectively) (Table 3). Also, there was no significant difference among the three exercise groups ( $p=0.338$ ).

## DISCUSSION

Isokinetic, aerobic, and isometric training for four weeks improved all clinical outcome variables including pain which was assessed according to the VAS, WOMAC, and Lequesne Index. Regarding the isokinetic strength measurements, the peak torque values of knee extension at 60° and 180°/sec angular velocities increased in all groups, and the highest change was in the isokinetic group. For the knee flexion peak torque values, improvements were significant only in the isokinetic group at both angular velocities. Morphological measurements of femoral and patellar cartilage using MRI revealed that the reductions observed after isokinetic training were not prominent enough to reach statistical significance. In the aerobic group, increments in both cartilage volumes were observed, rather than declines, although no statistical significance was reached. Interestingly, patellar cartilage volumes improved significantly in the isometric group, while the femoral cartilage volumes remained unchanged.

Our first hypothesis that isokinetic and aerobic exercises would increase the muscle strength at the expense of reduction in cartilage volume and both effects would be stronger after isokinetic exercise proved to be partially true. The flexion peak torques did not increase significantly in the aerobic group, as anticipated, but the expected reductions in cartilage volumes were unable to be achieved. Our second hypothesis that “isometric exercise would not alter the isokinetic muscle strength or cartilage morphology, but would reduce symptoms and increase the functional capacity” was unable to be fully met. Although isometric exercises improved the clinical outcome measures, unexpectedly, it also improved the extensor peak torque and patellar cartilage volume.

Currently, in the management of knee OA, complete cure of the disease cannot be achieved; however, modification of the disease is possible. Recommendations for the management of knee OA aim at reducing pain and physical disability, while limiting the structural joint deterioration.<sup>[26]</sup> Exercise is one of the most important non-pharmacological

treatment options which decrease pain and improve physical functions and is recommended in all of the guidelines developed for management of knee OA.<sup>[3-5,26]</sup> Although aerobic and resistance exercises have been shown to be beneficial, the optimal exercise type and frequency have not been clearly defined, yet.<sup>[4,5,26,27]</sup>

The quadriceps muscle has an important stabilizing role in maintaining the normal biomechanics of the knee. Weakness of the quadriceps muscle is common in knee OA due to disuse atrophy secondary to joint pain. On the other hand, quadriceps weakness is thought to be a risk factor for the progression of joint damage.<sup>[28-30]</sup> Isometric and isokinetic muscle strength measurements of the knee extension and also flexion in patients with knee OA have been shown to be lower than in healthy controls.<sup>[31]</sup> Strengthening exercises of the quadriceps and hamstring muscles may improve the joint stability.

Huang et al.<sup>[32]</sup> reported that isometric, isotonic, and isokinetic exercises decreased pain and disability, while increasing walking speed in patients with knee OA. The greatest improvement in walking speed, muscle strength, and physical function was observed after isokinetic exercises. However, Eyigor<sup>[33]</sup> demonstrated no superiority of isokinetic exercise over isotonic exercise in terms of walking speed and muscle strength. In our study, isokinetic exercise improved both flexor and extensor muscle strengths, whereas isometric and aerobic exercises improved the extensor muscle strength, but not the flexor muscle strength. Based on these findings, we suggest that isokinetic exercises may provide more benefits through effective stabilization with improvements in both agonist-antagonist muscle groups.

Knowledge about the effects of different types of exercise on cartilage morphology is important in the formulation of optimal exercise prescription in OA. Wijayaretne et al.<sup>[22]</sup> investigated the rate of annual patellar cartilage volume loss and its determinants in healthy middle-aged woman. They found that the annual loss of patellar cartilage volume was 1.6% in their patient group and participation in exercise tended to decrease rate of cartilage loss, but the type of exercise was not specified. Teichtahl et al.<sup>[23]</sup> also investigated the effect of vigorous physical activity on the patellar cartilage volume using MRI. After a two-year follow-up period, they found that vigorous physical activity reduced annual rate of the patellar cartilage volume loss particularly in healthy adults without any cartilage defects. They, therefore, concluded that weight-bearing vigorous

physical activity might be helpful in the prevention of knee OA. In both studies, the data regarding the exercise were obtained from the patients using a questionnaire.

In another study, Racunica et al.<sup>[11]</sup> investigated the effect of physical activity on the knee structures of healthy adults using MRI. They found that walking had a beneficial effect on the reduction of bone marrow lesions in the knee, but that had no effect on the tibial cartilage volume. The authors reported that previous or recent vigorous physical activity was associated with an increased tibial cartilage volume. Based on these findings, they concluded that vigorous physical activity had a protective effect on the knee cartilage. However, the amount of physical activity to produce this effect was not clearly specified. Similarly, data regarding the exercise were obtained using a questionnaire.

In addition, Gratzke et al.<sup>[20]</sup> found no significant difference in the cartilage thickness, except for the patellar cartilage in athletes, compared to the physically inactive participants. Weightlifters had a thicker patellar cartilage than untrained healthy individuals. Unique to all these studies, participants were healthy without any knee problems and they were evaluated based on preferred lifestyle, either physically active or inactive.

Cotofana et al.<sup>[34]</sup> also investigated the knee joint morphology after 12 weeks of endurance (cycling) and strength training to prove protection against knee OA in untrained middle-aged women without OA. They found no significant alterations in the cartilage thickness or volume using MRI. However, they showed a temporal relationship between exercise and cartilage morphology, although none of the participants were OA patients.

In a cross-sectional study conducted by Creaby et al.,<sup>[35]</sup> mechanical loading during walking might have a role in the pathological alterations in the articular cartilage in patients with OA. Different types of exercise result in different mechanical loading on the cartilage. In our study, four-week isokinetic, isometric, and aerobic exercise interventions did not have an unfavorable effect on the patellar or femoral articular cartilage, and isometric exercises even increased the patellar cartilage volume.

The main strength of the present study is that it is the first longitudinal study investigating the effects of different types of exercise on the cartilage morphology in patients with OA. A further strength of our study is

that all of the training sessions were performed under the supervision of a physiatrist. A potential strength of our study is the availability of an isokinetic exercise group, compared to the isometric and aerobic groups.

On the other hand, there are some limitations to this study. Longer duration of training interventions and the presence of a control group with no exercise intervention would strengthen our results. A second limitation was that tibial cartilage volume could not be measured and volumes of entire cartilage were measured without dividing into medial and lateral regions due to technical difficulties. These might lead to the underestimation of focal volume changes in case of non-uniform regional variations. The study is also limited by the inclusion only of women with OA; therefore, the results cannot be generalized to men or healthy adults.

In conclusion, isokinetic, aerobic, and isometric training for four weeks improved pain and functional capacity in patients with knee OA, without superiority of one type of exercise to another. Isokinetic exercise led to increments in the muscle strength measurements with improved maintenance of the quadriceps/hamstring ratio. We observed no significant unfavorable effect of any exercise type on the femoral or patellar cartilage volume. Only isometric exercise increased the patellar cartilage volume.

#### Declaration of conflicting interests

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

#### Funding

The costs of radiological assessments were funded by the Scientific Research Project Unit of Gazi University.

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