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EFFECTS OF A FOUR-WEEK HOME-BASED STRENGTHENING PROGRAM ON QUADRICEPS MUSCLE ARCHITECTURE IN RHEUMATOID ARTHRITIS AND KNEE OSTEOARTHRITIS: A PILOT STUDY

ABSTRACT

Purpose: To investigate changes in quadriceps femoris (QF) muscle architecture following a four-week home-based strengthening program in patients with rheumatoid arthritis (RA), knee osteoarthritis (OA), and healthy controls.

Methods: This prospective, non-randomized pilot intervention study included 12 patients with RA, 12 patients with knee OA, and 13 healthy controls. Ultrasonographic measurements of QF muscle thickness and pennation angle were obtained before and after a four-week home-based exercise program targeting the quadriceps and hamstring muscles. Functional outcomes were assessed using Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) and Lequesne scores in OA and Disease Activity Score in 28 joints with C-reactive protein (DAS28-CRP) in RA.

Results: Thirty-two participants completed the study (11 RA, 11 OA, and 10 healthy controls). At baseline, rectus femoris (RF) and vastus medialis (VM) thicknesses were significantly greater in healthy controls than in patient groups ($p=0.030$ and $p=0.036$, respectively). Following the intervention, significant increases in VM, RF, and vastus intermedius (VI) thickness were observed in the RA group, whereas RF and VI thickness increased in healthy controls. Pennation angles increased significantly in the vastus lateralis (VL), VM, and VI muscles in the OA group and in the VL and VM muscles in healthy controls. WOMAC and Lequesne scores improved significantly in OA (both $p<0.001$), whereas DAS28-CRP did not change significantly in RA ($p=0.481$). No significant between-group differences were detected after four weeks.

Conclusion: RF and VM thicknesses were lower in patients with RA and knee OA than in healthy individuals. Although significant within-group changes were observed, no significant between-group differences were detected following the intervention. Given the exploratory nature and limited sample size of this pilot study, these findings should be interpreted with caution.

Keywords: Arthritis, Exercise therapy, Knee, Osteoarthritis, Rheumatoid, Ultrasonography

ROMATOİD ARTRİT VE DİZ OSTEOARTRİTİNDE DÖRT HAFTALIK EV TEMELLİ GÜÇLENDİRME PROGRAMININ KUADRİSEPS KAS MİMARİSİ ÜZERİNE ETKİLERİ: PİLOT BİR ÇALIŞMA

ÖZ

Amaç: Romatoid artrit (RA), diz osteoartriti (OA) ve sağlıklı bireylerde dört haftalık ev temelli güçlendirme programı sonrasında kuadriseps femoris (KF) kas mimarisinde meydana gelen değişiklikleri araştırmaktır.

Yöntem: Bu prospektif, randomize olmayan pilot girişimsel çalışmaya 12 RA hastası, 12 diz OA hastası ve 13 sağlıklı kontrol dahil edildi. Kuadriseps ve hamstring kaslarını hedefleyen dört haftalık ev temelli egzersiz programı öncesinde ve sonrasında KF kas kalınlığı ve pennat açılımları ultrasonografi ile değerlendirildi. OA grubunda WOMAC ve Lequesne skorları, RA grubunda ise DAS28-CRP kullanıldı.

Bulgular: Çalışmayı toplam 32 katılımcı tamamladı (11 RA, 11 OA ve 10 sağlıklı kontrol). Başlangıçta rektus femoris (RF) ve vastus medialis (VM) kas kalınlıkları sağlıklı kontrollerde hasta gruplarına göre anlamlı olarak daha yüksekti (sırasıyla $p=0,030$ ve $p=0,036$). Müdahale sonrasında RA grubunda VM, RF ve vastus intermedius (VI) kas kalınlıklarında; sağlıklı kontrollerde ise RF ve VI kas kalınlıklarında anlamlı artış gözlemlendi. Pennat açıları OA grubunda [vastus lateralis (VL), VM ve VI] ve sağlıklı kontrollerde (VL ve VM) anlamlı olarak arttı. OA grubunda WOMAC ve Lequesne skorları anlamlı düzeyde iyileşirken (her ikisi için $p<0,001$), RA grubunda DAS28-CRP skorlarında anlamlı değişiklik saptanmadı ($p=0,481$). Dört hafta sonunda gruplar arasında anlamlı fark saptanmadı.

Sonuç: RA ve diz OA hastalarında RF ve VM kas kalınlıkları sağlıklı bireylere göre daha düşüktü. Her ne kadar bazı kas mimarisi parametrelerinde grup içi değişiklikler gözlemlenmiş olsa da, müdahale sonrası gruplar arasında anlamlı farklılık saptanmadı. Çalışmanın pilot niteliği ve sınırlı örneklem büyüklüğü nedeniyle bu bulgular dikkatle yorumlanmalıdır.

Anahtar Kelimeler: Artrit, Egzersiz tedavisi, Diz, Osteoartrit, Romatoid, Ultrasonografi



INTRODUCTION

Patients with rheumatoid arthritis (RA) often experience muscle atrophy and weakness due to joint motion impairment, peripheral neuropathy, chronic inflammation, and long-term corticosteroid therapy (1). Rheumatoid cachexia, which affects more than 50% of individuals with RA, further accelerates skeletal muscle loss (2). Knee joint involvement is common in RA, occurring in approximately 70-80% of patients, and contributes substantially to functional limitations (1).

Quadriceps femoris (QF) atrophy may develop even in the early stages of knee involvement (3). Individuals with RA exhibit reduced QF muscle strength and mass compared with age-matched healthy controls, which is closely associated with impaired physical performance and increased disability (4). Similarly, patients with knee osteoarthritis (OA) frequently demonstrate QF weakness—even when symptoms are relatively mild or absent—which is an important contributor to disease progression and functional decline (5).

Exercise-based interventions are an essential component of therapeutic approaches for both RA and OA. In RA, progressive resistance training has been shown to improve physical function, reduce disability, decrease the number of tender or swollen joints and enhance QF strength (6,7). In OA, deficits in QF sensorimotor function contribute to the degenerative cycle of pain, instability, and further joint damage, whereas resistance exercise helps to interrupt this cycle and restore neuromuscular control (8).

Muscle architecture comprises structural features such as cross-sectional area, muscle thickness, fascicle length, and pennation angle (9). Skeletal muscles demonstrate different architectural patterns—including fusiform and pennate configurations—each influencing functional capacity. In fusiform muscles, fibers run parallel to the longitudinal axis between the origin and insertion. In contrast, pennate muscles contain obliquely oriented fibers that insert onto a central tendon, forming a pennation angle (10). This angle, defined as the angle between the muscle fascicles and the deep aponeurosis (11), reflects how efficiently force produced by the muscle fibers is transmitted to the tendon; greater pennation angles are generally associated with improved mechanical efficiency and force production (12).

Previous studies have suggested that home-based exercise interventions may induce musculotendinous architectural adaptations. In healthy older adults, home-based exercise was associated with improvements in flexibility and increases in muscle fascicle length, indicating that structural adaptations may occur even in unsupervised settings (13). In clinical populations, home-based exercise programs have been shown to improve functional outcomes, muscle performance, and exercise participation in patients with RA (14). Furthermore,

home-based low-intensity resistance exercise has been reported to be feasible, safe and associated with high adherence in patients with RA and secondary sarcopenia (15). However, most available studies have focused on functional outcomes, flexibility, or muscle strength rather than quadriceps muscle architecture. Evidence regarding the effects of home-based exercise on ultrasound-derived quadriceps architectural parameters, particularly muscle thickness and pennation angle, remains limited, especially in patients with RA and OA. Given their accessibility, low cost, and potential to improve adherence to rehabilitation, home-based exercise programs represent an attractive option for clinical populations and warrant further investigation.

Although previous studies have demonstrated that resistance-based strengthening of the QF improves functional outcomes in both RA and OA, limited evidence exists on how short-term, combined QF-hamstring strengthening programs influence QF muscle architecture, particularly in RA populations. Therefore, the present pilot study aimed to explore changes in QF muscle thickness and pennation angle following a four-week home-based knee strengthening exercise program among individuals with RA, OA, and healthy controls, and to generate preliminary data to inform the design of future confirmatory studies.

METHOD

This prospective, non-randomized pilot intervention study was conducted at the Gazi University Hospital between October 2018 and June 2019. The primary aim of this pilot study was to explore potential changes in quadriceps muscle architecture following a short-term home-based strengthening program and to generate preliminary estimates of variability and potential effect sizes for future confirmatory studies. The study was not designed as a definitive efficacy trial. Sample size planning was based on a power level of 80% and a type I error rate of 5% (16). This calculation was used to guide recruitment planning; however, given the exploratory pilot nature of the study, it should not be interpreted as providing definitive statistical power for confirmatory between-group comparisons. A total of 37 participants were enrolled, including 12 patients with RA, 12 patients with knee OA, and 13 healthy controls.

Participant Selection

Patients with RA met the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism classification criteria, were 18-65 years old, and had no evidence of other inflammatory joint disorders. Patients with knee OA were diagnosed according to ACR criteria, and radiographic severity was graded as Kellgren-Lawrence stage 2 or 3 (17). Individuals with secondary OA or any concurrent inflammatory arthritis were excluded.

Healthy controls were volunteers without knee pain, lower-limb musculoskeletal disorders, or clinical signs of inflammatory or degenerative disease.

Exclusion Criteria

Exclusion criteria were standardized across groups and included:

- History of knee trauma, surgery, or intra-articular injection within the last six months,
- Neuromuscular or orthopedic conditions affecting the thigh (e.g., radiculopathy, myopathy, hip pathology),
- Secondary knee OA.

All participants provided written informed consent in accordance with the Declaration of Helsinki. The study protocol was approved by the Gazi University Institutional Ethics Committee (decision no: 673, date: 24.09.2018).

Clinical Evaluation

Demographic data (age, sex, height, body weight) were recorded for each participant. Disease duration was documented for the RA and OA groups. Baseline functional assessments were performed using the Western Ontario and McMaster Universities Osteoarthritis index (WOMAC), the Lequesne algofunctional index (for OA), and the Disease Activity Score in 28 joints with C-reactive protein (DAS28-CRP) for RA.

Ultrasound Assessment

Ultrasonographic evaluations of the dominant thigh were performed by an experienced physiatrist blinded to clinical data, using a MyLab 70 XV system (Esaote Biomedica, Genoa, Italy) equipped with a multi-frequency linear transducer in B-mode. Lower-limb dominance was defined as the limb used to kick a ball.

Measurements included muscle thickness and pennation angle for the vastus lateralis (VL), vastus medialis (VM), and vastus intermedius (VI), as well as the thickness of the rectus femoris (RF) and subcutaneous fat layer. Participants were positioned supine with neutral hip alignment and full knee extension. The transducer was placed perpendicular to the anterior thigh at the midpoint between the greater trochanter and lateral femoral condyle. All ultrasonographic measurements were performed by the same experienced examiner using the same ultrasound device and standardized anatomical landmarks. The transducer was positioned perpendicular to the skin surface, and minimal pressure was applied during image acquisition to reduce measurement variability.

Muscle thickness was measured as the vertical distance between the superficial and deep aponeuroses (18). Subcutaneous

fat thickness was defined as the distance between the skin-subcutaneous interface and the superficial RF aponeurosis (19). The pennation angle was defined as the angle between muscle fascicles and the deep aponeurosis (11) (Figure 1). Due to the nearly parallel fiber orientation of the RF, no pennation angle was computed for this muscle (18). Synovial proliferation and joint effusion were recorded as present or absent (20).

Exercise Intervention

Following baseline ultrasonography, all participants undertook a four-week home-based exercise program targeting the quadriceps and hamstring muscles. Before starting the intervention, participants received standardized exercise instruction through a face-to-face practical training session and written exercise materials.

The program consisted of quadriceps sets (A; isometric quadriceps contraction performed with the knee fully

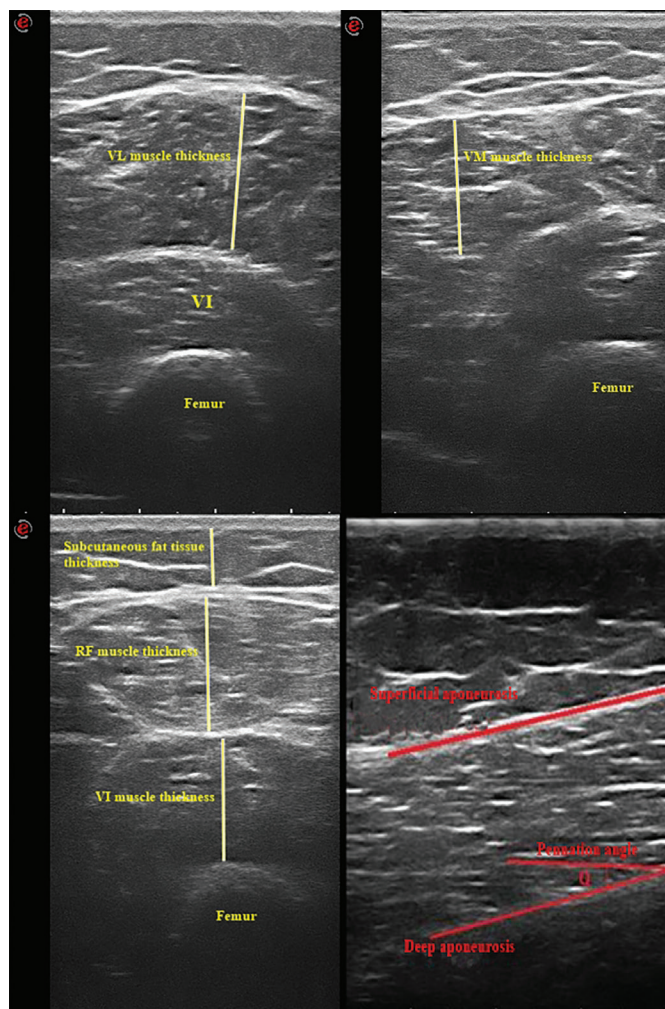


Figure 1. Sonographic thickness and pennation angle measurements.

RF: Rectus Femoris, VM: Vastus Medialis, VI: Vastus Intermedius, VL: Vastus Lateralis.

extended), straight-leg lowering exercises (B1-B4; controlled lowering of the extended lower limb through predefined positions), straight-leg raise exercises (C1-C2; active straight-leg elevation performed with the knee maintained in extension), quadriceps isometric exercises performed with the knee flexed to approximately 90° (D), hamstring sets (E; isometric hamstring contraction performed in the supine position), hamstring isometric exercises performed with the knee flexed to approximately 30° (F), and quadriceps-hamstring co-contraction exercises (G; closed-chain simultaneous contraction of the quadriceps and hamstring muscles) (21,22) (Figure 2).

Exercises were performed five days per week for four weeks. Each exercise consisted of two sets of 10 repetitions, and each contraction was held for 6-10 seconds. No progression in exercise intensity was implemented during the intervention period. Although the exercise program consisted predominantly of isometric exercises, straight-leg raise and straight-leg lowering exercises included dynamic movement components. These exercises were standardized through face-to-face instruction and written exercise materials provided to all participants. Participants were instructed to perform the exercises according to the demonstrations provided by the investigator and to maintain regular breathing while avoiding the Valsalva maneuver.

Adherence to the exercise program was encouraged through weekly telephone contact. Participants attended a follow-up visit at the end of the four-week intervention period, during which exercise completion was assessed based on participant self-report. Exercise intensity, contraction force, perceived exertion, and objective compliance measures were not formally recorded.

Reliability Analysis

To evaluate intra-observer reliability, muscle thickness and pennation angle measurements were repeated in seven healthy individuals (seven knees) one day apart by the same blinded observer using the same ultrasonographic protocol and anatomical landmarks. Intraclass correlation coefficients (ICCs) were calculated.

Rationale for Group Selection

Three groups were included to facilitate comparison of muscle morphology across an inflammatory joint disease (RA), a degenerative joint disease (OA), and healthy controls. Owing to the pilot and non-randomized nature of the study, between-group comparisons were considered exploratory.

Bias: To minimize potential sources of bias, all ultrasonographic assessments were performed by the same experienced physiatrist who was blinded to participants' clinical data. The

exercise protocol was standardized across all participants, and adherence was encouraged and monitored through weekly telephone contact. Baseline characteristics were compared across groups to identify potential baseline differences.

Statistical Analysis

Descriptive statistics were presented as mean $\pm$ standard deviation, median (interquartile range), or frequency and percentage, as appropriate. The distribution of continuous variables was assessed using the Kolmogorov-Smirnov test.

Baseline differences among the three groups were analyzed using one-way analysis of variance (ANOVA) for normally distributed variables or the Kruskal-Wallis test for non-normally distributed variables. Because disease duration was available only for the RA and OA groups, comparisons for this variable were performed using the Mann-Whitney U test. Within-group pre-post comparisons were performed using paired-sample t-tests for normally distributed data or Wilcoxon signed-rank tests for non-normally distributed data.

To explore differences in longitudinal changes among groups, change scores (post-intervention minus baseline values) were calculated for each outcome measure. Between-group comparisons of these change scores were performed using one-way ANOVA or the Kruskal-Wallis test, as appropriate. Table 1A and B present these change-score analyses. Given the pilot and exploratory nature of the study and the relatively small sample size, between-group analyses were considered hypothesis-generating rather than confirmatory.

Intra-observer reliability for repeated measurements of muscle thickness and pennation angle in the VL, VM, VI, and RF muscles was evaluated using ICCs.

All analyses were conducted using IBM SPSS Statistics version 22.0 (SPSS Inc., Chicago, IL, USA). A two-sided p-value of <0.05 was considered statistically significant.

RESULTS

A total of 37 participants were enrolled in the study. During the four-week intervention period, five participants were lost to follow-up or did not complete the post-intervention assessment. Consequently, 32 participants completed the study and were included in the final analysis: 11 individuals with RA, 11 with knee OA, and 10 healthy controls. Participant recruitment, follow-up, and inclusion in the final analysis are summarized in Figure 3. Their demographic and clinical characteristics are presented in Table 2A.

No significant differences were observed among the three groups in terms of age or sex distribution. The mean body mass index (BMI) was significantly higher in the OA group ($p=0.019$).

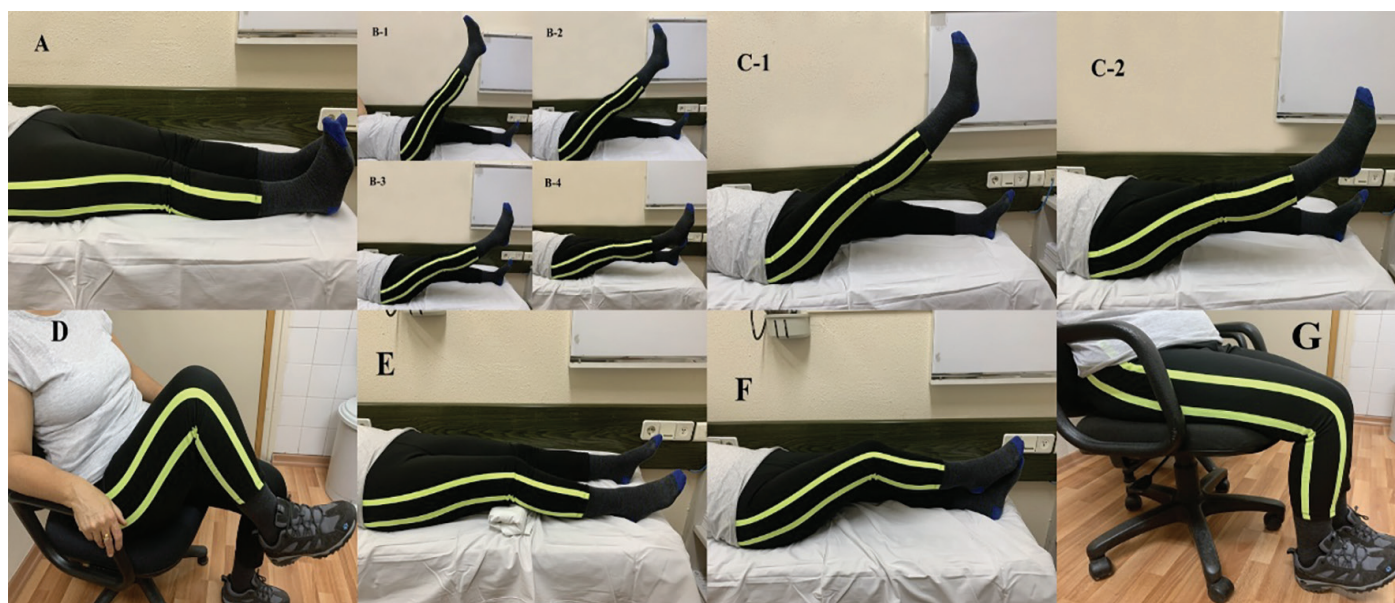


Figure 2. Quadriceps-Hamstring strengthening training. (A-D) Quadriceps isometrics. (A) Quadriceps sets, (B-1-4) straight-leg lowering, (C-1,2) straight-leg raise, (D) quadriceps multiple-angle isometrics. (E, F) Hamstring isometrics. (E) Hamstring sets, (F) hamstring multiple-angle isometrics. (G) Quadriceps-hamstring co-contraction training (closed-chain isometric).

Table 1A. Baseline and 1-month muscle thickness changes between groups

Baseline and 1 st month thickness difference (mm)	RA	Knee OA	Healthy	p-value
Vastus lateralis, mean $\pm$ SD	0.62 $\pm$ 1.37	0.75 $\pm$ 2.96	0.83 $\pm$ 1.29	0.974
Vastus medialis, mean $\pm$ SD	1.15 $\pm$ 1.32	0.02 $\pm$ 2.11	1.53 $\pm$ 2.31	0.197
Rectus femoris, mean $\pm$ SD	1.18 $\pm$ 1.45	0.24 $\pm$ 1.77	1.05 $\pm$ 1.24	0.309
Vastus intermedius, median (P ₂₅ -P ₇₅)	0.6 (0.2-1.8)	0 (0-1.7)	0.3 (0.6-1.2)	0.500
Subcutaneous fat tissue, median (P ₂₅ -P ₇₅)	1 (0.2-1.9)	1.4 (0.9-3.4)	1 (0.3-2.1)	0.526

Data are presented as mean $\pm$ SD or median (P₂₅-P₇₅), as appropriate. Data are presented as change scores (baseline to 1-month follow-up). Between-group comparisons were performed using one-way ANOVA or the Kruskal-Wallis test, as appropriate, as described in the Statistical Analysis section.

RA: Rheumatoid Arthritis, OA: Osteoarthritis, SD: Standard Deviation, ANOVA: Analysis of Variance.

Table 1B. Baseline and 1-month pennation angle changes between groups

Baseline and 1 st month pennate angle difference (°)	RA	Knee OA	Healthy	p-value
Vastus lateralis, mean $\pm$ SD	1.55 $\pm$ 3.86	4.64 $\pm$ 4.32	2.65 $\pm$ 3.21	0.179
Vastus medialis, median (P ₂₅ -P ₇₅)	1 (0-6)	4 (2-8)	2.25 (2-3)	0.237
Vastus intermedius, median (P ₂₅ -P ₇₅)	1 (-2-2)	2 (0-5)	0 (-3-5)	0.310

Data are presented as mean $\pm$ SD or median (P₂₅-P₇₅), as appropriate. Data are presented as change scores (baseline to 1-month follow-up). Between-group comparisons were performed using one-way ANOVA or the Kruskal-Wallis test, as appropriate, as described in the Statistical Analysis section.

RA: Rheumatoid Arthritis, OA: Osteoarthritis, SD: Standard Deviation, ANOVA: Analysis of Variance.

Median disease duration differed significantly, with 132 months in the RA group and 36 months in the OA group ($p=0.005$).

Baseline Ultrasonographic Findings

At baseline, healthy controls demonstrated greater VM and RF muscle thickness than the patient groups ($p=0.036$ and $p=0.030$, respectively) (Table 2B). No significant between-

group differences were observed for VL or VI muscle thickness ($p=0.160$ and $p=0.140$, respectively).

Pennation angles of the VL, VM, and VI did not differ significantly among the groups ($p=0.682$, $p=0.148$, and $p=0.256$, respectively).

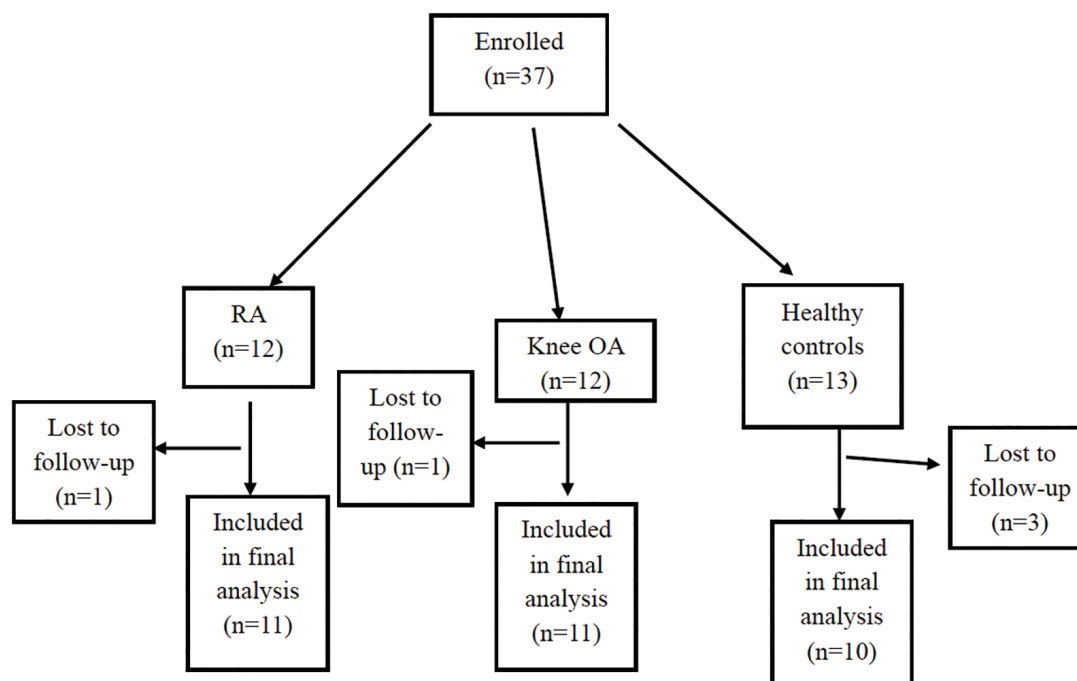


Figure 3. Flow diagram of participant recruitment, follow-up, and analysis.

RA: Rheumatoid Arthritis, OA: Knee Osteoarthritis.

Table 2A. Demographic data of groups

	RA	Knee OA	Healthy	p-value
Age (years), mean $\pm$ SD	53.5 $\pm$ 5	58.8 $\pm$ 6.3	55.2 $\pm$ 4.49	0.060
Gender, n (%)				0.059
Male	3 (25)	1 (7.7)	6 (46.2)	
Female	9 (75)	12 (92.3)	7 (53.8)	
BMI (kg/m ²), mean $\pm$ SD	28.1 $\pm$ 4.44	33 $\pm$ 6.3	27.9 $\pm$ 3.19	0.019
Disease duration (months), median (P ₂₅ -P ₇₅)	132 (72-168)	36 (24-72)		0.005

Data are presented as mean $\pm$ SD, median (P₂₅-P₇₅), or n (%), as appropriate. Group comparisons were performed using one-way ANOVA, Kruskal-Wallis test, or chi-square test, as appropriate. Disease duration was compared only between the RA and OA groups using the Mann-Whitney U test.

RA: Rheumatoid Arthritis, OA: Osteoarthritis, BMI: Body Mass Index, SD: Standard deviation, ANOVA: Analysis of Variance.

Table 2B. Baseline muscle thicknesses between groups

Baseline thickness (mm), mean $\pm$ SD	RA	Knee OA	Healthy	p-value
Vastus lateralis	16.4 $\pm$ 1.56	15.7 $\pm$ 2.55	17.3 $\pm$ 2.01	0.160
Vastus medialis	12.9 $\pm$ 1.05	12.3 $\pm$ 1.62	13.7 $\pm$ 1.27	0.036
Vastus intermedius	9.7 $\pm$ 0.82	10.1 $\pm$ 2.79	11.2 $\pm$ 1.65	0.140
Rectus femoris	13.6 $\pm$ 2.65	13.3 $\pm$ 2.79	16 $\pm$ 2.36	0.030
Subcutaneous fat tissue	16.8 $\pm$ 9.04	15.7 $\pm$ 6.5	11.7 $\pm$ 5.2	0.210

Data are presented as mean $\pm$ SD. Group comparisons were performed using one-way ANOVA.

RA: Rheumatoid Arthritis, OA: Osteoarthritis, SD: Standard deviation, ANOVA: Analysis of Variance.

Intra-Observer Reliability

ICC analysis demonstrated excellent intra-observer reliability for both pennation angle and muscle thickness measurements of the VL (pennation angle: ICC =0.94, $p=0.001$; thickness: ICC =0.92, $p=0.002$). Similarly, reliability was high for RF thickness (ICC =0.92, $p=0.001$) and for VI pennation angle (ICC =0.95, $p=0.003$).

The VM measurements also showed acceptable-to-high reliability (pennation angle: ICC =0.83, $p=0.026$; thickness: ICC =0.82, $p=0.016$). VI thickness demonstrated comparable reliability (ICC =0.81, $p=0.018$).

Clinical Outcomes

In the OA group, both the WOMAC and Lequesne indices improved significantly after the four-week intervention ($p<0.001$ for both) (Table 3). In contrast, the RA group showed no significant change in DAS28-CRP scores (baseline: 2.60 ± 0.87 ; post-training: 2.68 ± 0.87 ; $p=0.481$).

Changes in Quadriceps Muscle Thickness

In the RA group, significant increases were observed in VM ($p=0.016$), RF ($p=0.022$), and VI ($p=0.007$) muscle thickness, whereas VL thickness did not change significantly ($p=0.162$). Among healthy controls, RF and VI thickness increased significantly ($p=0.025$ and $p=0.008$, respectively), while changes in VL and VM did not reach significance ($p=0.073$ and $p=0.066$, respectively). No significant changes in muscle thickness were detected in the OA group (VL: $p=0.419$; VM: $p=0.967$; RF: $p=0.656$; VI: $p=0.165$).

Changes in Pennation Angle

In the RA group, pennation angles of VL, VM, and VI did not change significantly ($p=0.213$; $p=0.058$; $p=0.907$, respectively). Conversely, all pennation angles increased significantly in the OA group (VL: $p=0.005$; VM: $p=0.003$; VI: $p=0.012$). In healthy controls, significant increases were observed in VL and VM pennation angles ($p=0.028$ and $p<0.001$, respectively), while VI remained unchanged ($p=0.984$).

Synovial Findings

Synovial hypertrophy and joint effusion showed no significant differences among the groups at baseline or after the intervention.

Between-Group Comparisons

Between-group comparisons of change scores revealed no statistically significant differences among the groups for muscle thickness or pennation angle measurements (Table 1A and B). However, given the exploratory nature and limited sample size of this pilot study, these findings should be interpreted with caution.

Table 3. WOMAC/Lequesne scores

	Baseline	1 st month	p-value
WOMAC score, mean $\pm$ SD	32.7 $\pm$ 8.35	21.2 $\pm$ 8.32	<0.001
Lequesne score, mean $\pm$ SD	11.1 $\pm$ 3.06	7.9 $\pm$ 2.1	<0.001
Data are presented as mean $\pm$ SD. Within-group comparisons were performed using paired-sample t-tests. WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index, SD: Standard Deviation.			

DISCUSSION

The primary aim of this pilot intervention study was to explore changes in QF muscle architecture, particularly muscle thickness and pennation angle, following a four-week home-based strengthening program in individuals with RA, OA, and healthy controls. Our findings demonstrated that RF and VM muscle thickness were significantly greater in healthy participants than in both RA and OA groups. Although significant within-group changes were observed in some muscle architecture parameters following training, no statistically significant between-group differences were detected. Nevertheless, patients with knee OA demonstrated significant improvements in WOMAC and Lequesne scores following the intervention.

At baseline, notable differences were observed in RF and VM thicknesses across groups. Previous investigations have produced inconsistent results regarding which components of the QF undergo preferential atrophy in knee OA (23). In RA, most research has focused on VL atrophy, whereas comparative evaluations of multiple QF components remain limited in both human and animal studies (24). Type II fiber atrophy has been shown to predominate in both knee OA (25) and RA (26). Given that the RF is primarily composed of type II fibers (27), and the VM has been suggested to undergo selective type II fiber atrophy in knee OA due to pain, inflammation, and structural alterations (23), the reduced thickness of these muscles in RA and OA patients may reflect this preferential fiber loss. Moreover, previous work comparing VM biopsies in RA and OA reported no significant difference in type II fiber atrophy between these conditions (28), further supporting the observed pattern of reduced RF and VM thickness in patient groups compared with healthy controls.

Pennation angle reflects the alignment of muscle fibers relative to the tendon and is known to increase as contractile tissue becomes more densely packed within a given volume (18). Muscle atrophy may therefore decrease pennation angle due to loss of contractile density (29), although the association between cross-sectional area and pennation angle remains inconsistent (30). In contrast to some earlier studies, we did not observe significant baseline differences in pennation angle among groups. The heterogeneous and region-specific hypertrophic responses of QF components may account

for the variability seen in the literature (31). Differences in measurement techniques, anatomical regions assessed, and degrees of hypertrophy have also been cited as sources of discrepancy (9).

In this study, significant increases in QF muscle thickness were noted in all components except VL among participants with RA, and in the RF and VI muscles among healthy controls. These non-uniform adaptations likely reflect regional hypertrophy patterns within the QF. All pennation angles demonstrated an upward trend following training; however, between-group differences remained non-significant. Within-group analysis revealed significant increases in VL, VM, and VI pennation angles in the OA group, whereas only VL and VM showed significant changes in healthy controls. The literature presents diverging conclusions on how pennation angle responds to resistance exercise. Some investigators have reported proportional increases in pennation angle alongside muscle hypertrophy (30), while others found no such relationship (32,33). Even within the frequently studied VL, findings vary, with some studies reporting increased pennation angle after training, while others observed hypertrophy without angular changes. These inconsistencies suggest that pennation angle adaptations may differ not only between QF components but also across different regions of the same muscle (34).

The exercise protocol used in the present study incorporated multiple-angle isometric exercises and quadriceps-hamstring co-contraction exercises, which may have resulted in different loading and activation patterns across individual quadriceps components. Such differences may have contributed to the variable responses observed among the RF, VL, VM, and VI muscles. Furthermore, the inclusion of both predominantly isometric and dynamic exercise components may have increased the variability of muscle architectural responses. These factors may partly explain why significant changes were observed in some muscle parameters but not others.

The duration of training may also influence architectural adaptations. Although structural changes can begin within 4-6 weeks, longer or more intensive programs may be necessary to elicit consistent modifications in muscle architecture. This factor may help explain the absence of widespread architectural changes following the four-week intervention. Another factor that may have contributed to the limited architectural adaptations observed in the present study is the home-based nature of the exercise program. Exercise intensity, contraction force, and perceived exertion were not objectively quantified, and no progression in training load was implemented during the four-week period. Consequently, the mechanical stimulus may have been insufficient to induce consistent structural adaptations in quadriceps muscle

architecture, despite the functional improvements observed in some participants.

The interpretation of muscle architectural adaptations in RA requires consideration of disease-specific pathophysiological mechanisms. Rheumatoid cachexia and chronic inflammation have been associated with alterations in protein and energy metabolism, potentially influencing muscle mass and adaptive responses to exercise (2,35). Pro-inflammatory cytokines such as tumor necrosis factor- α , interleukin (IL)-1, and IL-6 may suppress anabolic pathways while promoting proteolysis (35). However, the patients included in the present study had low disease activity, with mean DAS28-CRP values within the remission range. Therefore, the influence of active systemic inflammation on muscle architectural adaptations may have been less pronounced in our cohort.

Previous research has demonstrated that resistance training can induce muscle hypertrophy in RA. Hakkinen et al. (36) reported that a 21-week QF resistance program increased maximal concentric and isometric knee extensor strength and QF thickness in both RA patients and healthy individuals. The magnitude of hypertrophy observed in RA appears comparable to that seen in healthy controls (37). Although fewer studies have examined the architectural response of QF muscles to resistance training in OA, one investigation found greater improvements in knee extensor strength in OA patients compared with healthy individuals after 13 weeks of dynamic resistance training (38). In the present study, no statistically significant between-group differences were detected in muscle thickness or pennation angle following the intervention. Given the exploratory nature and limited sample size of this pilot study, the absence of statistically significant between-group differences should not be interpreted as evidence of equivalent adaptive responses. Rather, these findings should be considered preliminary and hypothesis-generating. Larger adequately powered studies are required to determine whether true differences in muscle architectural adaptations exist among RA, OA, and healthy populations.

The OA group had a significantly higher BMI than the other groups. Increased adiposity may represent a potential confounding factor when interpreting muscle architecture measurements, as body composition can influence both muscle morphology and ultrasound-based assessments. However, subcutaneous fat thickness did not differ significantly among the groups in the present study. Nevertheless, the potential influence of BMI and body composition on muscle thickness measurements and architectural outcomes cannot be completely excluded and should be considered when interpreting the findings.

The functional benefits of QF strengthening program for knee OA—including pain reduction, improved function,

and enhanced postural control—are well documented (39). Consistent with the literature, both WOMAC and Lequesne scores improved significantly in the OA group following training. These improvements may be attributed to enhanced QF strength, decreased extension deficits, and improved proprioceptive input (40). Future research could explore the physiological mediators of these functional gains in individuals with knee OA.

The clinical significance of the observed ultrasonographic changes remains uncertain, as correlations between changes in muscle architectural parameters and functional outcome measures were not evaluated. Future studies should investigate whether alterations in muscle thickness and pennation angle are associated with improvements in pain, physical function, and patient-reported outcomes.

Limitations

This study has several limitations. We did not assess architectural adaptations of the hamstring muscles, despite their involvement in the intervention program. Additionally, the short duration of the training may have limited the magnitude of architectural change detectable via ultrasound. Long-term follow-up studies are needed to determine whether structural adaptations in QF architecture are sustained or progress over time. Furthermore, the non-randomized design and lack of allocation concealment limit internal validity; therefore, between-group comparisons should be interpreted as exploratory. The relatively small final sample size may also have limited the statistical power to detect subtle between-group differences, increasing the possibility of type II error. In addition, exercise intensity, contraction force, perceived exertion, and objective adherence measures were not formally recorded. Therefore, the relationship between training load and the observed muscle architectural changes could not be fully evaluated. Detailed medication data, including Disease-Modifying Antirheumatic Drug biologic therapies, and corticosteroid use, were not systematically evaluated in the present analysis. Physical activity levels outside the prescribed exercise program were not systematically monitored, and dietary intake was not controlled. In addition, participant blinding was not feasible because all participants were aware of the exercise intervention they were performing. These factors may have influenced the observed outcomes and should be considered when interpreting the findings. Additionally, muscle architecture measurements were obtained from a single anatomical site for each muscle. Given the known regional heterogeneity of quadriceps muscle architecture, single-site measurements may not fully reflect whole-muscle structural adaptations. Furthermore, intra-observer reliability was assessed only in healthy participants; therefore, the reliability of ultrasound measurements in patients with

RA and OA remains uncertain. In addition, correlations between changes in muscle architectural parameters and clinical outcome measures were not analyzed. Therefore, the functional relevance of the observed ultrasonographic changes could not be determined. Future research should investigate the relationship between architectural changes and isokinetic muscle strength outcomes, incorporate objective monitoring of exercise intensity and adherence, evaluate the reliability of ultrasonographic measurements in patient populations, and account for the potential influence of medication use on muscle architectural adaptations.

CONCLUSION

In this pilot study, RF and VM muscle thicknesses were significantly lower in patients with RA and knee OA than in healthy individuals. Following a four-week home-based strengthening program targeting the quadriceps and hamstrings, participants with knee OA demonstrated improvements in pain and physical function, whereas disease activity in patients with RA remained unchanged. No statistically significant between-group differences in muscle architectural parameters were detected following the intervention; however, given the exploratory nature and limited sample size of this pilot study, these findings should be interpreted with caution and should not be considered evidence of equivalent adaptive responses among the groups. Future studies incorporating objective monitoring of exercise intensity, adherence, and progression are needed to better clarify the relationship between training load and muscle architectural adaptations in RA and OA.

Ethics: The study protocol was approved by the Gazi University Institutional Ethics Committee (decision no: 673, date: 24.09.2018).

Informed Consent: All participants provided written informed consent in accordance with the Declaration of Helsinki.

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