Acute Effects of Walking on The Deformation of Femoral Articular Cartilage

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ACUTE EFFECTS OF WALKING ON THE DEFORMATION OF

FEMORAL ARTICULAR CARTILAGE

By

Jayson McClaren

Skyler Sudweeks

A doctoral project submitted in partial fulfillment

of the requirements for the

Doctor of Physical Therapy

Department of Physical Therapy

School of Allied Health Sciences Division of Health Sciences

The Graduate College

University of Nevada, Las Vegas

May 2017
Doctoral Project Approval

The Graduate College
The University Of Nevada, Las Vegas

May 1, 2017

This doctoral project prepared by

Jayson McClaren and Skyler Sudweeks

entitled

Acute Effects of Walking on the Deformation of Femoral Articular Cartilage

is approved in partial fulfillment of the requirements for the degree of

Doctor of Physical Therapy

__________________________________________  __________________________
Research Project Coordinator  Graduate College Dean

__________________________________________  __________________________
Research Project Advisor  Chair, Department of Physical Therapy

ABSTRACT

Background and Purpose: Knee osteoarthritis (OA) is characterized by a progressive loss of the articular cartilage, increasing the amount of friction in the joint, resulting in pain and decreases in mobility and function. Additionally, it has been demonstrated that frontal plane lower extremity (LE) malalignment (e.g., varus, valgus) is associated with onset and progression of OA. Previous studies showed that static loading of 50% body weight at the knee results in more cartilage deformation in those with knee OA compared to healthy controls. As walking produces forces in the knee that are 2-3 times body weight, it may result in greater cartilage deformation. The purpose of our study was to compare the acute effects of walking on the femoral cartilage deformation between individuals with and without knee OA and determine whether LE alignment is associated with greater cartilage deformation.

Subjects: 10 subjects without OA (5 females and 5 males; 55.0 ± 1.8 yrs; 78.8 ± 14.0 kg; 1.8 ± 0.2 m) and 9 subjects with OA were recruited (4 females and 5 males; 55.6 ± 4.5 yrs; 97.4 ± 15.0 kg; 1.7 ± 0.1 m).

Methods: Each subject underwent X-ray and MRI assessment. For X-ray assessment, persons with Kellgren/Lawrence grades 2-3 were assigned to the OA group whereas subjects with grades 0-1 were assigned to the control group. During MRI assessment, 3T, frontal-plane MRI was obtained before and immediately after 30 minutes of treadmill walking at 3-4 mph. LE alignment was obtained by measuring the angle between the long axes of femur and tibia using a goniometer. To obtain cartilage deformation post-walking, the medial and lateral femoral cartilage of the weight-bearing areas were segmented on subjects’ MRI. Cartilage thickness was quantified by computing the perpendicular distance between opposing voxels defining the edges
of the femoral cartilage. Cartilage volume was quantified by multiplying the segmented area by slice thickness. Independent t-tests were used to compare cartilage deformation (i.e., percent changes in medial and lateral cartilage thickness/volume) in response to walking between the 2 groups. Pearson correlation coefficients were used to assess the association between cartilage deformation and LE alignment of all subjects.

Results: Independent t-tests revealed no significant difference in percent change of cartilage thickness between OA group and control group in medial (p=0.873) or lateral (p=0.688) femur. Additionally, there was no difference in percent change of cartilage volume between the two groups in medial (p=0.159) or lateral (p=0.327) femur. Pearson correlation coefficient analyses revealed a significant correlation between reductions in lateral femoral cartilage thickness and increased knee valgus alignment (p=0.030).

Conclusion: This is the first study assessing the acute effects of walking on femoral cartilage deformation between persons with and without knee OA. Although there was not a difference in cartilage deformation between persons with and without OA, it was found that knee valgus was related to lateral femoral cartilage deformation in response to walking.

Key Words: Knee Osteoarthritis, Cartilage
ACKNOWLEDGEMENTS

This research study was made possible by the Graduate & Professional Student Association Grant and the University of Nevada, Las Vegas Physical Therapy Department Grant. The authors would like to thank Kai-Yu Ho PT, Ph.D for her excellent guidance as principle investigator of this study, William Roddy McGee, MD for imaging referrals, and Szu-Ping Lee, PT, Ph.D for additional support with this project.
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INTRODUCTION

Osteoarthritis (OA) most often affects the knee joint and is the most common cause of knee pain in adults ages 50 and older. It is estimated that 12.1% of Americans have symptomatic knee OA, a number that continues to rise. Progression of knee OA could result in disability and affect an individual's participation in society and independent living. Economically, this poses an ever-increasing financial burden on society. The average per-person direct medical costs associated with symptomatic knee OA have been estimated to be $19,600 over their lifetime. Risk factors for developing OA include increased body mass index (BMI), previous knee injury, female gender, and older age. Additionally, it has been reported that frontal plane knee alignment (e.g., varus and valgus) is associated with onset and progression of uni-compartmental OA. In persons with knee OA, both varus and valgus malalignment increased the risk of progression in the medial and lateral compartment respectively. Janakiramanan et al. found that for every 1° increase towards genu valgum, an individual has an increased risk for the development of lateral compartment cartilage defects.

Articular cartilage, which covers the ends of long bones and allows them to glide over each other with little friction, consists of type II collagen fibers, water, proteoglycans, and glycosaminoglycans. With OA, a progressive loss of articular cartilage occurs, increasing friction in the joint. It has been proposed that osteoarthritic cartilage has a lower content of proteoglycans and collagen fibers, as well as reduced collagen fibril connectivity and fibril orientation when compared to healthy cartilage. This degeneration of cartilage can result in pain, decreased mobility, and decreased function, and often leads to a decrease in activity.
Although there is no cure for OA, there are many treatment options available to help manage pain. Treatments that have been shown to be effective are physical therapy, weight reduction, acupuncture, transcutaneous electrical stimulation and pharmalological treatment such as analgesics, non-steroidal anti-inflammatory drugs (NSAIDs), and disease-modifying osteoarthritis drugs (DMOADs).18–21

Cartilage obtains its nutrition from synovial fluid inside the joint.22 The synovial fluid also provides lubrication of the joint during compression and allows it to roll and/or glide with minimal to no pain. A systemic review paper concluded that physical activity has at least short term benefits of reduced pain and increased physical function in those with knee OA. 23 Because compression lubricates the joint, walking is commonly suggested in the management of knee OA. The Arthritis Foundation advocates walking for 30-60 minutes each day, 3-5 days per week.24,25 Other programs have similar recommendations;26 however, these recommendations are primarily based on subjective outcome reports of pain and improved function following walking. Although walking can reduce pain and increase physical function in those with knee OA, Hurwitz et al.27 found that pain relief resulting from pharmalological intervention increased loading of the degenerative areas of the articular cartilage. This leads us to believe that the analgesic effects of walking could also contribute to further degeneration of the articular cartilage.

With the advancement of medical technology and better imaging procedures, articular cartilage has become quantifiable with the use of magnetic resonance imaging (MRI); however, results of cartilage thickness vary between studies.1,28,29 Cotofana et al.1 compared the differences in tibiofemoral cartilage thickness in elderly females upon static loading at 50% body weight.
was found that healthy individuals had a deformation of 2.8±2.6%. Subjects with a diagnosis of minimal knee OA and moderate knee OA had a deformation of 4.3±2.2% and 5.3±4.5% respectively. With the static load of 50% body weight, the deformation nearly doubled between OA versus non-OA groups. Dynamic loading, such as walking, has been demonstrated to load the knee joint 2-3 times body weight.\textsuperscript{30,31} With a load that is 5-6 times greater than that used by Cotofana \textit{et al.}, there is a potential for even greater deformation. To the best of our knowledge, there are no studies on the acute effects that walking has on femoral cartilage thickness in individuals with knee OA compared to individuals without knee OA.

The primary purpose of this research was to determine the percent reduction of distal femoral cartilage deformation (thickness and volume) in response to an acute bout of mechanical loading (i.e., walking) between healthy individuals and individuals that have been medically diagnosed with knee OA. We aimed to determine how joint loading during walking and lower extremity (LE) alignment affects cartilage deformation. It was hypothesized that individuals who have knee OA would exhibit increased femoral cartilage deformation than individuals without knee OA in response to an acute bout of walking. We also hypothesized that increased cartilage deformation would be associated with LE malalignment in persons with and without OA.
METHODS

Subjects

Nine subjects with radiographically-confirmed knee OA (4 females and 5 males; 55.6 ± 4.5 yrs; 97.4 ± 15.0 kg; 1.7 ± 0.1 m) and 10 subjects without radiographically-confirmed knee OA were recruited (5 females and 5 males; 55.0 ± 1.8 yrs; 78.8 ± 14.0 kg; 1.8 ± 0.2 m) (Table 1). The data from an existing study was used to estimate the sample size for detecting a difference in cartilage thickness changes between persons with and without knee pathology.\(^{32}\) Using a two-sided paired t-test with 80% power and \(\alpha\) value of 0.05, the analysis estimated that 9 individuals in each group would be needed to detect a group difference in cartilage deformation.

In order to participate in the study, subjects must meet these criteria: 1) 50-65 years old, 2) able to safely walk at least 3 miles per hour continuously for 30 minutes, 3) pain less than 5/10 on pain numeric rating scale (NRS) during walking if taking pain medication OR pain less than 7/10 on NRS during walking if not taking pain medication. The pain level during walking was controlled as pain may influence their gait patterns and walking ability. Subjects were excluded from participation if they reported having any of the following: 1) a history of surgical procedure performed to the knee that could alter the musculoskeletal integrity of the knee, 2) implanted biological devices that could interact with the magnetic field, 3) current cancer/tumor or history of cancer/tumor, 4) are pregnant/think they may be pregnant, or 5) risk for performing moderate physical activity as reported on Physical Activity Readiness Questionnaire (PAR-Q).\(^{33}\) Subjects’ physical activity levels were determined based on the World Health Organization’s Global Physical Activity Questionnaire.\(^{34}\) This questionnaire has been reported to provide a valid and reliable estimate of physical activity.\(^{35}\) Prior to participation, all subjects were informed of the
nature of the study and signed a consent form approved by the Institutional Review Board of the University of Nevada, Las Vegas (IRB# 764521-3).

Table 1. Subject characteristics (mean ± standard deviation). * indicates a statistical significance (p<0.05).

<table>
<thead>
<tr>
<th></th>
<th>OA group (n=9)</th>
<th>Control group (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>55.6 ± 4.5</td>
<td>55.0 ± 1.83</td>
<td>0.725</td>
</tr>
<tr>
<td>Height, m</td>
<td>1.73 ± 0.07</td>
<td>1.75 ± 0.15</td>
<td>0.674</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>97.4 ± 15.0</td>
<td>78.8 ± 14.1</td>
<td>0.013*</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>32.4 ± 4.35</td>
<td>25.49 ± 2.98</td>
<td>0.001*</td>
</tr>
<tr>
<td>Activity level, MET.min/week</td>
<td>3137.8 ± 3137.5</td>
<td>1520 ± 1640.3</td>
<td>0.171</td>
</tr>
<tr>
<td>Kellgren/Lawrence Grade</td>
<td>2.3 ± 0.5</td>
<td>0.3 ± 0.48</td>
<td>0.000*</td>
</tr>
<tr>
<td>Alignment, degrees</td>
<td>177.6 ± 4.13</td>
<td>177.4 ± 3.98</td>
<td>0.934</td>
</tr>
<tr>
<td>NRS of pain before walking</td>
<td>0.2 ± 0.44</td>
<td>0 ± 0</td>
<td>0.128</td>
</tr>
<tr>
<td>NRS of pain during walking</td>
<td>1.67 ± 1.87</td>
<td>0.1 ± 0.32</td>
<td>0.018*</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>112.6 ± 7.3</td>
<td>117.5 ± 10.9</td>
<td>0.265</td>
</tr>
<tr>
<td>Walking speed (m/sec)</td>
<td>1.40 ± 0.1</td>
<td>1.48 ± 0.1</td>
<td>0.165</td>
</tr>
</tbody>
</table>

Procedure

Data collection occurred in 2 separate days (Day 1: X-ray Assessment; Day 2: MRI Examination) with approximately 1-2 weeks apart.
X-ray Assessment

On Day 1, subjects underwent an X-ray of both knees in standing. Joint space narrowing and osteophytes were assessed in both knees to determine the group assignments (OA and Control). Contracted radiologists evaluated both knees to determine OA according to the Kellgren/Lawrence (K/L) Grading Scale for each subject. Persons with K/L grading of 2-3 (moderate degenerations) were assigned to the OA group and persons with K/L grading of 0-1 were assigned to the control group. K/L grade 0 is defined as no joint space narrowing or reactive changes; K/L grade 1 is defined as doubtful joint space narrowing and possible osteophyte lipping; K/L grade 2 is defined as definite osteophyte formation with possible joint space narrowing; K/L grade 3 is defined as moderate osteophytes, definite joint space narrowing, some sclerosis, and possible bone-end deformity.

For the subjects in the OA group, the knee with more evidence of OA was assessed in the MRI examination session. If both knees had the same grade of OA, the dominant knee (defined as the limb they prefer to land on from jumping) was studied. The limb evaluated in the control subjects was either the limb with the smallest K/L grade or was matched to that of their gender-match counterpart in the OA group.

MRI Examination

MRI data was collected using a 3.0 T MRI scanner (Titan Model MRT 3010, Software version...
2.5xR001, Toshiba America Medical Systems, Inc., Tustin, CA) along with a 16-channel flex speeder medium coil (Neocoil, Pewaukee, WI). This session took subjects approximately 90 minutes each to complete. Upon arrival, a LE alignment of the leg was measured, which is defined as the angle between the long axis of the femur and the long axis of the tibia. The body height and weight was also measured. Participants were then placed in a wheelchair with their legs elevated to unload the knee joint for a minimum of 30 minutes. This is performed to avoid any external compression of the knee joint that can affect cartilage deformation.

Following joint unloading, subjects were asked to report their pain using a NRS pain scale and then were transferred to the scanner for their pre-walking MRI. A 3-D, coronal-plane, fast spoiled gradient recalled echo (SPGR) sequence MRI protocol was applied to the knee joint (TR = 17 ms, TE = 3 ms, flip angle = 4°, matrix = 456 X 512, FOV = 160 X 180 mm, slice thickness = 2 mm, scan time = 30 seconds). After completion of the pre-walking MRI, participants were instructed to walk on a treadmill (Gold’s Gym Trainer 420 treadmill) at a fast speed between 3 to 4 mph for 30 minutes similar to a previous study by Ho et al. The fast walking speed was defined as the highest speed within 3 to 4 mph that a subject achieved without the presence of double limb swing or reported physical discomfort. The subjects were instructed to walk fast, but were allowed to change the speed if necessary. Immediately following the walking session, participants reported their pain using the NRS and returned to the scanner to receive their post-walking MRI using the same MRI sequence described previously. The time from completion of walking to the initiation of the post-walking MRI was approximately 2-3 minutes.

Data Analysis
**Cartilage Thickness/Volume Measurement**

Cartilage thickness and volume were obtained by using 3 steps of analysis. Thickness and volume were quantified as both variables are studied in existing literature.\(^1\),\(^2\),\(^41\),\(^42\) First, the image slices that contained weight-bearing regions of bones were identified. Specifically, the weight-bearing area on each condyle was defined using the method established by Blazek et al.\(^42\) as the region bounded anteriorly by the medio-lateral line intersecting with the lowest point of the cartilage in the trochlea and extending 60% of the distance to the most posterior point of the articular cartilage covering each condyle (Figure 1). After the weight-bearing slices were identified, medial and lateral cartilage of the femur were manually segmented by a single investigator using a commercial software package (sliceOmatic, Tomovision, Montreal, QC, Canada) (Figure 2). Differentiation between the medial and lateral femoral cartilage was determined by the investigator at the point to where there was no identification of cartilage in the region of the intercondylar eminence.\(^41\) Lastly, thickness was quantified by computing the perpendicular distance between opposing voxels defining the edges of the femoral cartilage using a custom Matlab program (Mathworks, Natick, MA, USA).\(^32\) Cartilage volume was quantified by multiplying the segmented area by slice thickness using the mathematical algorithms embedded in sliceOmatic. It should be noted that the single trained investigator responsible for cartilage measurements was blinded to group assignment (OA or Control) and scan conditions (pre- or post-walking) during cartilage segmentation.
Figure 1. Identifying the weight bearing regions of the femur.

Figure 2. Segmentation of femoral cartilage. The center of the femoral trochlea was used to divide the medial (green) and lateral (red) cartilage.
**Frontal plane LE angle**

Frontal plane LE angle was utilized to measure varus or valgus alignment of the knee. Frontal plane alignment was defined as the angle between the long axis of the femur and the long axis of the tibia. This was assessed by using the method described by Kraus et al.,\(^3\text{8}\) in which the centers of the patella, ankle, and thigh were marked with a pen. The center of the goniometer was placed on the center of the patella and the arms of the goniometer were aligned with the center of the thigh and lower leg to the center of the ankle (Figure 3). An angle smaller than 180° was defined as valgus alignment of the knee, whereas an angle greater than 180° was defined as varus alignment.\(^3\text{8}\) All LE alignment measurements were performed by the same investigator.

![Figure 3. Measurement of the frontal plane knee alignment: (A) The measurement landmarks (midpoint of the thigh, center of the patella, and midpoint of the ankle) were demonstrated. The lateral angle was used to describe the knee alignment; (B) The placement of goniometer.](image)
Measurement Reliability

The primary outcome measures included 1) thickness of femoral cartilage (medial and lateral); 2) volume of femoral cartilage (medial and lateral); 3) frontal plane LE angle. To establish intrarater reliability of each outcome measure, the investigators performed repeated measurement of 5 subjects at 2 days (with 7 days apart). Intraclass correlation coefficients (ICCs) and standard errors of measurement (SEM) were used to assess the reliability of the investigator between day 1 and 2. For LE alignment, the investigator demonstrated an excellent measurement reliability (ICC = 0.932) with a low SEM of 0.929°. Additionally, the investigator showed excellent intrarater reliability in the measurement of cartilage thickness (ICC ranging from 0.918-0.973 and SEM of 0.0635-0.159 mm) and volume of medial and lateral femur (ICC ranging from 0.940-0.952 and SEM ranging from 5.974-13.10 mm3).

Statistical analysis

Prior to statistical analyses, all variables were assessed for normality and found to be normally distributed based on results of the Shapiro-Wilk test. Independent t-tests were used to compare percent changes in medial and lateral cartilage thickness and volume in response to walking between individuals with OA and controls. Pearson correlation coefficients were used to assess the association between changes in cartilage deformation (thickness and volume) and frontal plane LE angles of all subjects. All statistical analyses were performed with use of SPSS 22.0 statistical software (International Business Machines Corp., Armonk, NY, USA). A significant level was set as 0.05.
RESULTS

Subject Characteristics

As indicated in Table 1, participants with OA had significantly higher body weight, BMI, K/L grading, and pain level during walking when compared to healthy controls (p<0.05). In addition, both groups showed similar age, height, LE alignment, physical activity level, and cadence and speed during the 30-minutes walking session (p>0.05). The reported activity level indicated that both groups are moderately active.\

Cartilage Deformation after Walking

The findings of independent t-tests showed that there was no significant change in cartilage thickness post-walking between individuals with and without OA of the medial femur (p=0.873) or lateral femur (p=0.688) (Figure 3; Table 2). Independent t-tests also showed no significant change in cartilage volume post-walking between groups of the medial femur (p=0.159) and lateral femur (p=0.327) (Figure 4; Table 2).
Table 2. Comparisons of femoral cartilage deformation after walking between persons with and without OA.

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Post-walking</th>
<th>Percentage Change</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OA</td>
<td>Control</td>
<td>OA</td>
<td>Control</td>
</tr>
<tr>
<td>Femoral Cartilage Thickness, mm</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>1.59 ± 0.30</td>
<td>1.51 ± 0.21</td>
<td>1.55 ± 0.28</td>
<td>1.48 ± 0.25</td>
</tr>
<tr>
<td>Lateral</td>
<td>1.54 ± 0.20</td>
<td>1.54 ± 0.20</td>
<td>1.50 ± 0.25</td>
<td>1.51 ± 0.18</td>
</tr>
<tr>
<td>Femoral Cartilage Volume, mm³</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medial</td>
<td>1424 ± 271</td>
<td>1338 ± 323</td>
<td>1375 ± 219</td>
<td>1341 ± 341</td>
</tr>
<tr>
<td>Lateral</td>
<td>1402 ± 175</td>
<td>1418 ± 323</td>
<td>1379 ± 234</td>
<td>1430 ± 292</td>
</tr>
</tbody>
</table>

Figure 4. Comparison of percent changes in femoral cartilage thickness after walking between persons with and without OA.
Figure 5. Comparisons of percent changes in femoral cartilage volume after walking between persons with and without OA.

**Associations between Change in Cartilage Thickness and Frontal Plane LE Alignment**

The findings of the Pearson correlation coefficient analyses indicated no significant correlation between changes in cartilage thickness of the medial femur and increased varus alignment (R=0.273, p=0.257), whereas a significant moderate correlation was found between changes in cartilage thickness of the lateral femur and valgus alignment (R=0.497, p=0.030) as shown in Table 3. Figures 5 and 6 show the Pearson correlation between LE alignment and changes in cartilage thickness in response to walking.

**Table 3.** The associations between LE alignment and % change in femoral cartilage thickness *indicates a statistical significance (p<0.05)

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial Femoral Cartilage</td>
<td>0.273</td>
<td>0.257</td>
</tr>
<tr>
<td>Lateral Femoral Cartilage</td>
<td>0.497</td>
<td>0.030*</td>
</tr>
</tbody>
</table>
Figure 6. Correlation between LE alignment and change in medial cartilage thickness.

Figure 7. Correlation between LE alignment and change in lateral cartilage thickness.

Associations between Change in Cartilage Volume and Frontal Plane LE Alignment
The findings of the Pearson correlation coefficient analyses indicated that there was no significant correlation between changes in cartilage volume of the medial femur and knee varus alignment (R=0.104, p=0.671). There was no significant correlation found between changes in cartilage volume of the lateral femur and knee valgus alignment (R=0.309, p=0.197) as shown in Table 3. Figures 7 and 8 show the Pearson correlation between LE alignment and changes in cartilage volume in response to walking.

Table 4. The associations between LE alignment and % change in cartilage volume.

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medial Femoral Cartilage</td>
<td>0.104</td>
<td>0.671</td>
</tr>
<tr>
<td>Lateral Femoral Cartilage</td>
<td>0.309</td>
<td>0.197</td>
</tr>
</tbody>
</table>

Figure 8. Correlation between LE alignment and change in medial cartilage volume.
Figure 9. Correlation between LE alignment and change in lateral cartilage volume.
DISCUSSION

To the authors’ knowledge, this is the first study assessing the acute effects of walking on the deformation of femoral articular cartilage of the knee. The primary purpose of this research was to determine the relative percent reduction of distal femoral cartilage deformation (thickness and volume) in response to an acute bout of mechanical loading (i.e., walking) between healthy individuals and individuals that have been radiographically diagnosed with knee OA. Our findings did not support our hypothesis that individuals with knee OA would exhibit more femoral cartilage deformation than individuals without knee OA after walking. However, in support of our secondary hypothesis, genu valgum was found to be associated with reduction in cartilage thickness of the lateral femur after walking.

The existing literature has revealed conflicting evidence regarding the acute effects of mechanical loading on tibiofemoral cartilage deformation, likely due to different loading status (static or dynamic), loading frequency, and/or loading duration being used among the studies. For instance, Cotofana et al.\textsuperscript{1} reported a difference in cartilage deformation between persons with and without OA after 45 minutes of static loading at 50\% body weight. On the contrary, Van Ginckel et al.\textsuperscript{43} investigated the acute effects of a squat exercise on the tibiofemoral cartilage between healthy individuals and those with knee OA and found no significant change between groups in cartilage deformation. It should be noted that cartilage deformation depends on loading frequency. When the frequency is low, or intermittent, the cartilage can easily adapt; however, when the frequency is high, or static, the cartilage cannot respond quickly and results in increased deformation.\textsuperscript{44} Although walking has been demonstrated to load the knee joint 2-3
times body weight, the biomechanical properties of cartilage combined with an intermittent loading frequency during walking did not result in increased cartilage deformation in our study.

When compared to the cartilage deformation percentage of our study to that of a dynamic, intermittent activity (i.e., squatting) reported by Van Ginckel et al., a smaller percentage of deformation in both OA and control groups were reported in our study (see Table 2). Van Ginckel et al. reported a 3.4%-3.9% reduction in femoral cartilage volume after squatting whereas we found a 1.9-2.9% decrease in femoral cartilage volume after walking. Walking and squatting have been reported to cause similar peak resulting forces at the tibiofemoral joints (walking 261% body weight; squatting: 253% body weight). One possible explanation as to why we observed a smaller deformation amount in response to an acute bout of mechanical loading was due to decreased ground reaction force (GRF) resulting from a cushioned effect provided by the treadmill. The foundation of the treadmill was designed to create a cushioned effect, which the manufacturer claims reduces impact on joints. The cushioned effect decreases the GRF placed on the weight bearing joints of the LE. This decrease in GRF results in a decrease in compression forces applied through the knee and in turn decreases the amount of deformation occurring in the femoral articular cartilage.

Our results demonstrated that the OA group had significantly more pain than the control group during walking (Table 1), which might contribute to the insignificant findings of the femoral cartilage deformation between the 2 groups. We suspected that pain may have led to altered gait mechanics of the OA group. Mundermann et al. found that those with knee OA exhibited altered gait mechanics (e.g., Trendelenburg gait) to redistribute the load in the knee joint. It is possible that the participants who had pain while walking altered the mechanics of their gait to
redistribute forces in the knee. Altering forces in the knee joint could reduce the amount of
femoral articular cartilage deformation observed in the OA group.

A secondary aim of the study was to determine whether frontal plane LE knee angle is associated
with reduced distal femoral cartilage thickness/volume in response to an acute bout of
mechanical loading (i.e., walking) in individuals with and without knee OA. Our findings
demonstrated that knee valgus alignment was correlated with increased percent change of lateral
femoral cartilage thickness. It has been demonstrated that in knees with OA, both varus and
valgus knee alignment increased the risk of OA progression in the medial and lateral
compartments, respectively.9–11 Our findings were supported by Janakiramanan et al.12 who
showed that every 1 degree increase in knee valgus is associated with an increased risk of lateral
cartilage defects of the tibiofemoral joint. In the current study, we did not observe an association
between medial cartilage deformation and varus alignment. This may be due to the fact that the
majority of our selected cohort had valgus alignment (13 out of 19).

With respect to the findings of the current study, 3 major limitations should be recognized. First,
the results of the present study should be interpreted in view of the relatively small sample size.
The small sample size limits the generalizability of the results to a broader population. Second,
although participants were asked to return to the MRI scanner immediately after walking, the
preparation time (including subject setup and MRI localizing scans) took 2-3 minutes. Such
preparation time might cause some recovery of the tibiofemoral cartilage, however, this time gap
is comparable to prior studies with similar MRI methods.46,47 Third, we did not control for
subjects’ footwear during walking as subjects were asked to wear the shoes they usually wear for
exercises or walking. As it has been found that both the type of shoe48 and presence/type of
insole\textsuperscript{49,50} can contribute to a significant decrease in GRF, the footwear may have an effect on the cartilage deformation.
CONCLUSION

This is the first study assessing the acute effects of walking on femoral cartilage thickness between persons with and without knee OA. Our data revealed that walking did not significantly decrease cartilage thickness in participants with and without OA. However, we found that knee valgus was related to lateral femoral cartilage deformation in response to walking. Our research suggests that walking on a treadmill for 30 minutes at a speed of 3-4 mph did not alter femoral cartilage deformation for individuals aged 50-65 with knee OA. This research may impact the interventions for individuals with knee OA. Nonetheless, future research should continue to investigate cartilage deformation after walking and consider the long-term effects of walking on cartilage deformation.
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