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The Relationship Between External Knee Moments and Muscle Co-Activation in Subjects with Medial Knee Osteoarthritis

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Abstract

Purpose: External knee moments are reliable to measure knee load but it does not take into account muscle activity. Considering that muscle co-activation increases compressive forces at the knee joint, identifying relationships between muscle co-activations and knee joint load would complement the investigation of the knee loading in subjects with knee osteoarthritis. The purpose of this study was to identify relationships between muscle coactivation and external knee moments during walking in subjects with medial knee osteoarthritis. *Methods:* 19 controls (11 males, aged 56.6 ±5, and BMI 25.2 ± 3.3) and 25 subjects with medial knee osteoarthritis (12 males, aged 57.3 \pm 5.3, and BMI 28.2 \pm 4) were included in this study. Knee adduction and flexion moments, and co-activation (ratios and sums of quadriceps, hamstring, and gastrocnemius) were assessed during walking and compared between groups. The relationship between knee moments and co-activation was investigated in both groups. Findings: subjects with knee osteoarthritis presented a moderate and strong correlation between co-activation (ratios and sums) and knee moments. Interpretation: Muscle co-activation should be used to measure the contribution of quadriceps, hamstring, and gastrocnemius on knee loading. This information would cooperate to develop a more comprehensive approach of knee loading in this population.

1. Introduction

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Knee osteoarthritis (KOA) is one of the most common musculoskeletal diseases in the UK and has been estimated to affect over 12.5% of the UK population (Peat et al. , 2001, Yu et al. , 2015). Knee load has been considered one of the most important factors related to the onset and progression of the disease. Additionally, the knee load on the medial compartment has been emphasized as it is more affected than the lateral compartment (Ledingham et al. , 1993). For this reason, external knee adduction moment (EKAM) has been used as a surrogate for medial knee load, given its strong association with medial and lateral load ratio and disease progression (Hurwitz et al. , 1998, Miyazaki et al. , 2002, Sharma et al. , 1998, Shelburne et al. , 2006, Zhao et al. , 2007). It is well established that EKAM is higher in subjects with medial KOA when compared with a control group (Baliunas et al. , 2002, Hurwitz et al. , 2002, Hurwitz et al. , 2000, Mills et al. , 2013, Sharma, Hurwitz, 1998).

Even though EKAM is considered as a predictor of medial knee compartment load, its behaviour alone does not necessarily reflect the behaviour of the medial knee compartment (Walter et al. , 2010). For instance, a reduction in EKAM can be associated with an increased knee flexion moment (KFM), which is also detrimental to the knee cartilage (Chehab et al. , 2014). Although an increased KFM may affect both knee compartments, it has an important contribution to understanding the medial knee load (Manal et al. , 2015) as it is responsible for progression of the disease in specific regions of the medial compartment (Chehab, Favre, 2014). In addition, knee adduction angular impulse (KAAI) has been considered as another important measure of medial knee compartment. It takes into account the magnitude of the EKAM and the duration of this variable throughout the stance phase (Thorp et

al., 2006). Moreover, KAAI has been associated with disease progression (Bennell et al., 2011), pain, and disability (Kito et al., 2010). For this reason, not only EKAM but also KFM and KAAI should be considered to better understand the behaviour of medial knee compartment loading.

Knee load is not only determined by kinetic and kinematic variables, but also by muscle forces generated around the knee joint (Sasaki and Neptune, 2010, Winby et al., 2013). For instance, the guadriceps, hamstrings, and gastrocnemius act during the stance phase to control the joint and consequently have an important contribution to the knee joint loading (Winby et al., 2009). The co-activation of these muscles is an important measure to explore their role in generating forces around the knee joint. Recently, a study (Hodges et al., 2016) found a positive association between the duration of medial co-activation and medial cartilage loss, and also an inverse association between lateral co-activation and medial cartilage loss. Coactivation is defined as the simultaneous activation of agonist and antagonist muscle groups around a joint (Levine and Kabat, 1952). Co-activation can be measured as: (1) generalised, when all agonists and antagonists are activated equally, and (2) specific or directed, when medial and lateral muscles are activated separately (Heiden et al., 2009). In subjects with KOA, co-activation has been pointed out as increased due to higher muscle activity (Hubley-Kozey et al., 2009, Zeni et al., 2010); however, there is no consensus in the literature. For instance, a study (Lewek et al., 2004) found higher co-activation between the medial quadriceps and medial gastrocnemius in subjects with KOA, while another study (Schmitt and Rudolph, 2007) found higher co-activation between the lateral quadriceps and lateral gastrocnemius. In addition, the disease severity seems to influence the co-activation

as higher co-activation was found in subjects with severe KOA when compared to a control group, while moderate KOA showed higher co-activation only between the lateral quadriceps and lateral gastrocnemius (Hubley-Kozey, Hill, 2009). Based on the findings described above, it is clear that studies are needed to clarify whether co-activation between the quadriceps, hamstrings and gastrocnemius is higher in subjects with KOA compared to a control group. In addition, it is important to explore both types of co-activation, and generalised and specific ratios.

Considering that knee joint loading is one of the main factors related to the onset and progression of the disease (Baliunas, Hurwitz, 2002, Chang et al., 2015, Chehab, Favre, 2014, Felson, 2013), the combination of knee joint moments and muscle co-activation would be an approach to better understand the behaviour of knee joint load (Winby, Gerus, 2013, Winby, Lloyd, 2009). On the one hand, EKAM, KFM and KAAI are well established variables for measuring knee loading, mainly on the medial knee compartment. On the other hand, there is no well-established specific or generalised co-activation ratio for measuring the role of muscles in the knee joint loading. For instance, a study (Heiden, Lloyd, 2009) found an association between medial-lateral co-activation and external knee moments (peak EKAM and KFM) in KOA subjects. However, the authors did not specify the location of OA in their subjects, which is important information given specific co-activation may be related to the location of OA. In addition, using an electromyography-driven model in subjects who had undergone an arthroscopic partial meniscectomy, a study (Winby, 2013) found a small relationship between KFM and generalised Gerus, (hamstring:quadriceps) and lateral specific (vastus lateralis:lateral hamstring and vastus lateralis:lateral gastrocnemius) co-activation. Considering these potential

findings and the lack of studies using subjects with medial KOA, investigating the relationship between muscle co-activation and external knee moments would help to determine which muscle co-activation ratios should be used to measure the contribution of muscles to the knee joint load. This information would help in understanding the behaviour of knee load considering not only knee joint moments but also muscle contribution. Thus, the objectives of this study were to (1) compare external knee moments, and quadriceps, hamstring, and gastrocnemius co-activation between subjects with KOA and a control group; (2) identify relationships between muscle co-activation and external knee moments in both groups. We hypothesised that KOA subjects would present higher knee moments and muscle co-activation between external knee moments and muscle co-activation between external knee moments and muscle co-activation in the control group.

2. Methods

2.1 Subjects

Forty-four subjects were included in the study (Table 1). Participants were recruited from the community through advertisements in the local media. All subjects underwent anteroposterior semi-flexed weight-bearing, lateral view, and skyline view radiographs. The volunteers were assessed according to the criteria of Kellgren and Lawrence (KL) (Kellgren and Lawrence, 1957) as only mild and moderate KOA were included. Using the anteroposterior knee radiographs we measured the lower limb alignment as described previously (Colebatch et al. , 2009). The participants were diagnosed as KOA if they met the American College of Rheumatology (clinical, radiographic and history) criteria (Altman et al. , 1986). In addition, only subjects with

predominantly medial KOA were included, therefore subjects were excluded if they presented the same or greater KL grades in the lateral or patellofemoral compartment than those in the ipsilateral medial compartment (Zeni, Rudolph, 2010). In the same way, we included only subjects with predominantly medial knee pain as we used the WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) pain subscale for this evaluation. Subjects were excluded when they presented higher pain level in the lateral knee compartment and/or patellofemoral joint. The control group demonstrated no evidence of radiological and/or clinical signals of KOA. Volunteers were excluded if they presented any of the following criteria: body mass index greater than 35kg/m², history of hip or knee arthroplasty or osteotomy, or if they had undergone knee surgery or other nonpharmacological treatment in the 6 months prior to the study (Kean et al., 2015). Considering the criteria described above, we evaluated 40 subjects with knee pain, however, 15 subjects were excluded as two presented a unilateral positive test for ACL injury, two had important low back pain (more pain in their back than knee), two presented hip pain, and the other nine subjects presented other compartments as affected as or more affected than the medial knee compartment (7 in the PFOA and 2 in the lateral knee compartment). In addition, we evaluated 23 subjects without knee pain, two were excluded as they had a BMI> 35 kg/m², while two presented KOA in the radiographic exam but no pain was present. Ethics approval was obtained from the institutional ethics committee and all participants provided written informed consent.

2.2 Gait evaluation

An eight-camera Qualisys Oqus 300 motion analysis system (Qualisys, Gothenburg, Sweden) and two force plates (Bertec Corporation, OH, USA) were

used to record kinematic and kinetic data at sampling frequencies of 120 and 1200 Hz, respectively. Volunteers walked barefoot at a self-selected speed along an 8 m walkway. For each subject, a static calibration trial, followed by five successful trials were collected for EMG, kinetic, and kinematic analysis. A trial was considered successful when the subject walked naturally landing with the whole foot of the affected limb on the covered force plate (Chapman et al., 2015).

The following reflective markers were located on anatomical landmarks bilaterally: acromia, iliac crests, anterior and posterior superior iliac spines, greater trochanters of the femur, medial and lateral femoral epicondyles, medial and lateral malleoli, first, second and fifth metatarsal heads, base of the fifth metatarsal, and calcaneus. A single marker was placed on the sternal notch and spinous process at C7. Four clusters built with 4 noncollinear markers were placed over the lateral side of the right and left thigh and shank. Two additional clusters built with 3 noncollinear markers were positioned on the spinous process at T4 and T12. The medial and lateral malleolus, femoral condyles, seventh cervical vertebrae, greater trochanters, and acromion process were removed after the static standing calibration trial was performed. These markers were used to construct the anatomical coordinate system for the trunk, pelvis, thigh, shank, and foot segments. The ankle and knee joint centres were calculated as midpoints between the malleoli and femoral condyles, respectively (Chapman, Parkes, 2015). The hip joint centre was measured using the regression model based on the anterior and posterior superior iliac spine markers (Bell et al., 1989). The angular motion of all assessed joints was defined using Cardan angles in accordance with the recommendations of the International Society of Biomechanics (Wu et al., 2002).

The kinetic and kinematic data were processed using Qualisys Track Manager (Qualisys AB) and Visual3D software (C-motion Inc., Rockville, MD, USA). The kinetic and kinematic data were filtered using a fourth-order, zero-lag, low-pass Butterworth filter at cut-off frequencies of 6 and 25 Hz, respectively. External knee moments were calculated using three-dimensional inverse dynamics and were normalized to the product of weight and height (%Bw*Ht). In addition, KAAI was normalized by the weight, height, and time (%Bw*Ht*s). The KAAI, first peak EKAM, second peak EKAM, and peak KFM were analysed during the stance phase. The most affected leg was used for all measures in the KOA group and a side was selected randomly for the control group.

2.3 EMG co-activation ratio and sum

Myoelectric activity was recorded at 1200Hz using a Trigno[™] Wireless System (Delsys Inc., Boston, USA) and surface EMG electrodes, Trigno[™] Wireless Sensor (Delsys Inc., Boston, USA). The EMG electrodes contained four silver (99.9%) bar contacts (5 x 1 mm), an overall channel noise of <0.75uV, and a Common Mode Rejection Ratio (CMRR) >80 dB. The subject's skin surface was prepared by shaving and abrading with alcohol wipes and water solution. Sensors were attached on the skin surface (Delsys® Adhesive Sensor Interface), according to the position of the muscle belly and perpendicular to the muscle fibre direction for maximum signal detection as recommended by SENIAM (Hermens et al. , 2000). Myoelectric activity was recorded from the vastus medialis (VM), vastus lateralis (VL), rectus femoris (RF), biceps femoris (BF), medial gastrocnemius (MG), and lateral gastrocnemius (LG). The amplitude of myoelectric activity was normalized to the amplitude of the myoelectric activity obtained during the maximal voluntary

isometric contraction (MVIC). Prior to the tests to measure the MVIC, participants were positioned and asked to perform sub-maximal contractions for warm-up and familiarisation with the exercise. The quadriceps MVIC was performed in a supine position at 45° knee flexion. A strap (attached to the floor) was wrapped around the ankle, another strap was used to maintain the pelvis against the table, and a foam roller was positioned under the knee to maintain it flexed. The lateral hamstring MVIC was performed at 15° knee flexion in the supine position. A strap was wrapped around the ankle and another secured the pelvis against the table. Finally, the medial and lateral gastrocnemius MVICs were performed in a prone position, with neutral plantar flexion. A strap (attached to the floor) was wrapped around the forefoot and participants were asked to push the strap using their forefoot. Another strap was used around their pelvis to maintain the pelvis against the table. Three MVIC tests were performed for each muscle group (quadriceps, biceps femoris, and gastrocnemius) with a rest interval of 60-seconds between each trial. The average maximum value from each of the three trials was used for normalization.

The EMG data were processed using Visual 3D software (C-Motion Inc., Rockville, USA). Raw EMG data were band-pass filtered (20-450 Hz), full wave rectified and then filtered with a zero lag, fourth order, 6Hz low pass Butterworth filter to create linear envelopes. In order to calculate the co-activation, the average of EMG amplitude of each muscle normalized by the MVIC was used. The EMG data were also normalized to 101 points throughout the stance phase (IC to toe-off). In addition, we calculated the co-activation throughout the whole and early stance phase (0-32% of stance phase). The co-activation during the early stance phase (0-32%) includes the first peak of EKAM and KFM, while the co-activation throughout

the whole stance phase includes the same peaks and also the second peak of EKAM, KFM, and gastrocnemius activity. For our analysis, we considered previously described measures for co-activation (Heiden, Lloyd, 2009): (1) agonist and antagonist ratio activation, (2) activation sum of agonist and antagonist and (3) dominant determination of agonist and antagonist. Moreover, the maximum coactivation ratio is represented as zero, while minimum co-activation is indicated as 1 or -1 (co-activation ratio is positive when agonist is higher than antagonist and viceversa). In the present study, the following ratios and sums were measured: VM:MG, VL:LG, VL:BF, EXT(VM,VL,RF):FLX(BF,MG,LG), QUA(VM, VL):GAST(MG,LG). The within-session reliability of data was performed for EMG recordings and MVIC of VM, RF, VL, BF, MG, and LG. A two-way mixed model was used to calculate the intraclass correlation coefficient (ICC) within trials. The average measure with 95% confidence interval (CI) and coefficient of variation (CV) were calculated in order to demonstrate the reliability of the mean of recordings. The ICC values of EMG recordings and MVIC were higher than 0.80, ranging from 0.87 to 0.99 for EMG recordings and from 0.88 to 0.98 for MVIC measures. The CV values ranged from 9 to 24% for EMG recordings and from 11 to 32% for MVIC.

2.4 Statistical analysis

First, the data distribution and homogeneity of variance were analyzed using the Shapiro-Wilk and Levene's tests, respectively. Second, descriptive measures (mean and SD) were obtained for each variable. Differences between groups (control x KOA) were analyzed using independent samples t-tests to compare age, weight, height, BMI (body mass index), gait speed, WOMAC (Western Ontario & McMaster Universities Osteoarthritis Index) questionnaire (total, pain, stiffness, and

physical function score) (table 1), and external knee moments (KAAI, KFM, first, and second EKAM). As the assumption of normality for EMG data was violated, we performed a Mann-Whitney U test to compare co-activation (ratios and sums) between groups.

The Spearman rank test was performed for correlation analysis between coactivation and external knee moments for both groups. The level of correlation was determined using the following values: <0.3 represented weak correlation, from 0.3 to 0.7 moderate correlation, and >0.7 strong correlation (Bland and Altman, 1995). Co-activation variables could be positive or negative (from 1 to -1) and the closer to zero the higher the co-activation. Considering this information, it would be difficult to interpret the results after a correlation test as a positive and negative correlation would mean different results. For this reason, we classified co-activation into ordinal variables as low (3), moderate (2), and strong (1) co-activation. Values from 0 to 0.33 or from 0 to -0.33 were classified as strong co-activation, values from 0.34 to 0.66 or from -0.34 to -0.66 were classified as moderate co-activation, and from 0.67 to 1 or from -0.67 to -1 were classified as low co-activation. Using this classification it is possible to appropriately analyze the relationships between the knee moments and muscle co-activation as positive or negative.

Finally, considering that muscle is an important contributor to knee load and a correlation was found between external knee moments and muscle co-activation, an ANCOVA was used to compare external knee moments between groups, accounting for specific co-activation ratios and sums. The ANCOVA model for each knee moment variable (KAAI, first and second peak EKAM) was processed individually accounting for significantly correlated co-activation ratios and sums. Statistical

3. Results

A total of forty-four volunteers were included in the study and there were no differences between controls and KOA subjects regarding age, height, body mass, or gait speed (Table 1). KOA subjects presented a higher BMI, varus alignment, pain, stiffness, disability, and total score than the control group (Table 1).

"Insert table 1 here"

KOA subjects displayed a higher KAAI (P=0.007), and first (P=0.001) and second (P<0.001) peak of EKAM than controls. The KFM was not different between groups (Figure 1).

"Insert Figure 1 here"

The co-activation was not significantly different between groups for any ratio or sum during the stance phase (Figure 2) or during the early stance phase (Figure 3).

"Insert Figure 2 here"

"Insert Figure 3 here"

Throughout the stance phase there was a negative correlation of the VL:BF ratio, VM:MG sum, and QUA:GAST sum co-activations with KAAI, first, and second peak of EKAM (Table 2) in the KOA group only. A negative correlation was found between QUA:GAST co-activation ratio and KAAI and the second peak of EKAM (Table 2) in the KOA group only. In addition, a positive correlation was found

between VM:MG sum and KAAI and second peak of EKAM in the control group (Table 2). No correlation was found between co-activation during the early stance phase and external knee moments (Table 3) for both groups.

"Insert Table 2 here"

"Insert Table 3 here"

In order to measure the contribution of muscles for knee loading, we performed an ANCOVA test between groups comparing external knee moments, accounting for significantly correlated co-activation ratios and sums. For KAAI and second peak of EKAM, we used four co-activations as covariates (VL:BF and QUA:GAST ratios, and VM:MG and QUA:GAST sums), however, the KOA group still displayed a higher KAAI (P=0.02) and second peak of EKAM (P<0.001). The comparison between groups showed a significant influence of VL:BF and QUA:GAST ratios for KAAI (P=0.004 and P=0.009 respectively) and second peak of EKAM (P=0.006 and P=0.03). For first peak of EKAM, we used four co-activations (VL:BF ratio and VM:MG, QUA:GAST, and EXT:FLX sums). Although the VL:BF ratio presented a significant influence (P=0.02) on the first peak of EKAM, the KOA group still presented a higher value in comparison to the control group (P=0.003).

4. Discussion

This study proposed to compare the external knee moments (EKAM, KFM, and KAAI) and co-activation (ratios and sums) between KOA subjects and a control group, and, to investigate whether there is an association between these measures. We confirmed other reports that KOA subjects present higher KAAI and EKAM (first and second peaks) however, no difference was found between groups for KFM or

co-activation (ratio and sum). Moreover, we found a moderate and strong correlation between co-activation and knee adduction moments in the KOA group but no correlation for the control group.

The EKAM and KAAI have been used as surrogates for medial knee load (Hurwitz, Ryals, 2002, Sharma, Hurwitz, 1998, Weidenhielm et al., 1994, Zhao, Banks, 2007) as well as associated with disease progression (Bennell, Bowles, 2011, Chehab, Favre, 2014, Sharma, Hurwitz, 1998) and severity (Kean et al., 2012) in patients with KOA. For this reason, it was not surprising to find a greater EKAM and KAAI in the KOA group since we included only medial KOA subjects, confirming the same findings found by previous studies (Baliunas, Hurwitz, 2002, Hurwitz, Ryals, 2002, Hurwitz, Ryals, 2000, Lewek, Rudolph, 2004, Miyazaki, Wada, 2002, Sharma, Hurwitz, 1998, Weidenhielm, Svensson, 1994). Furthermore, the KFM was not significantly different between groups, which may be explained by our sample being composed of medial KOA subjects. A recent study (Teng et al., 2015) found a higher peak of KFM during the second half of the stance phase in subjects with patellofemoral OA, which means that KFM may be related to patellofemoral OA. Even though KFM combined with EKAM can improve understanding of medial knee load (Manal, Gardinier, 2015), KFM in isolation explains only 22% of medial contact force and for this reason must be cautiously interpreted in KOA subjects.

Co-activation has been considered as a mechanism where synergistic and antagonist muscles around a joint are simultaneously recruited (Falconer and Winter, 1985, Sirin and Patla, 1987). In our study, there were no differences between groups for any co-activation ratio or sum. In contrast to our findings, another study (Hubley-Kozey, Hill, 2009) found a greater co-activation ratio in a severe KOA group

compared with an asymptomatic group, using similar ratios (VM:MH, VM:MG, VL:BF, VL:LG) as the present study. In addition, the authors found significantly higher coactivation in severe KOA subjects in comparison with the moderate KOA group only for the VL:BF ratio. This contrast between our results and those of Hubley-Kozey et al. may be due to the severity of the disease and ages of the samples. While we included only subjects classified as mild and moderate KOA (II and III according to the KL scale) matched by age, their findings were shown in a more severe group (IV according to the KL scale) compared to a significantly younger control group. As older people normally display higher co-activation then younger people (Billot et al., 2014), their results may have been influenced by age. In addition, muscle activity alterations are related to the severity of osteoarthritis (Rutherford et al., 2013), the higher the severity the higher the co-activation. This information would explain our results as the majority of our participants (68%) had an early degree of KOA (II according to the KL scale) and our groups were matched by age. Therefore, greater co-activation seems to be related to the late stages of the disease (Hubley-Kozey, Hill, 2009) and older people.

Although no difference was found between groups for co-activation ratios or sums, the KOA group displayed a higher medial knee load when compared to the control group. Considering that quadriceps, hamstrings, and gastrocnemius are important contributors to knee loading, the higher medial knee load in the KOA group may be related to the lower limb alignment. For instance, Hurwitz el al. (Hurwitz, Ryals, 2002) found that mechanical axis of the lower limb explains 53 and 56% of the variation in the first and second EKAM, respectively, which may explain our findings as the KOA group showed a higher varus alignment than the control group

(P= 0.03). Although no difference in co-activation was found between groups, significant correlations were found between external knee moments and co-activations. Interestingly, most of these correlations were found only in the KOA group, only two relationships were found in the control group (VM:MG sum with KAAI (r=0.50) and second EKAM (r=0.50)) which could represent muscle adaptation to the disease; however, as this is a cross-sectional design study, we cannot state this possibility.

It is noteworthy that the strong correlation was between lateral co-activation (BF:VL ratio) and medial knee load (KAAI and first EKAM), which means that the higher the medial knee load, the higher the lateral co-activation. Possibly, this correlation represents a good strategy. As an example, a recent study (Hodges, van den Hoorn, 2016) showed that increased duration of lateral co-activation is inversely related to medial compartment cartilage loss, which represents a protection against medial compartment cartilage loss. However, as this is a cross-sectional study, we cannot affirm that this is a protective mechanism in subjects with KOA. In addition, we found that the quadriceps and gastrocnemius ratio (QUA:GAST) was inversely correlated with KAAI (r= -.41) and second peak of EKAM (r= -.53), which is explained by the behaviour of quadriceps and gastrocnemius activity during walking. For instance, while quadriceps is mainly activated during the first 50% of stance phase, gastrocnemius is mainly activated during the second 50% of stance phase (Winby, Gerus, 2013).

In the present study, we also investigated the correlation between coactivation sums and external knee moments. Co-activation sums represent the sum of all agonist and antagonist activity. Based on our findings, the higher the co-

activation sum of VM:MG (r= -.42, -.47, and -.50) and QUA:GAST (r= -.47, -.55, and -.51) the higher the medial knee load (KAAI, first, and second peak of EKAM, respectively). In addition, the higher the EXT:FLX co-activation sum the higher the first peak of EKAM (r=-.49). Similar results were found by Winby et al. (2013), as they observed an association between the co-activation sum of VM:MG and medial knee load ($R^2 = 0.53$). Moreover, the authors found a correlation between the sum of VL:LH co-activation and lateral load ($R^2 = 0.50$). Despite the VM:MG co-activation sum presenting a significant correlation with medial knee load in both studies, we used three-dimensional inverse dynamics and subjects with medial KOA, while the other study used an EMG-driven model to predict the knee load and subjects who had undergone an arthroscopic partial meniscectomy. Surprisingly, no correlation was found between external knee moments and the co-activation during the early stance phase. Although this phase involves the peak EKAM and KFM, we used the mean of agonist and antagonist muscle groups to process the co-activation ratios (Heiden, Lloyd, 2009), which may not be a representative measure of muscle contribution for knee loading.

As external joint moments do not account for the contribution of muscles (Heiden, Lloyd, 2009, Schipplein and Andriacchi, 1991), these co-activation ratios and sums can be used to measure their contribution. In order to complement this information, the ANCOVA test was performed using correlated co-activation variables as covariates. For KAAI and second peak EKAM, two co-activation ratios (VL:BF and QUA:GAST) demonstrated a significant influence but the KOA group still displayed higher values than the control group. In the same way, for first peak EKAM, the VL:BF ratio presented a significant influence, however, the KOA group

still displayed a higher value. Based on these findings, it is clear that there is an important contribution of quadriceps, hamstring, and gastrocnemius co-activation on knee loading; however, it is not possible to affirm that they are responsible for the higher knee load in the KOA group as no difference for co-activation between groups was found. It is noteworthy that the main contribution of this study was to highlight co-activation ratios and sums that should be used to measure the muscle contribution for knee loading. In the same way, these co-activations can be used to measure the effect of an intervention. For instance, a pilot study (Al-Khlaifat et al., 2016) found a reduction in the VL:BF ratio after a six week intervention in subjects with KOA. Similarly, a recent study (Preece et al., 2016) found a reduction in medial co-activation (medial quadriceps:medial hamstring) after an intervention using the Alexander Technique. Despite these two studies finding a reduction in different coactivation ratios, they attributed this reduction to an improvement in symptoms. For this reason, the use of co-activation measures could help in understanding the effect of an intervention on knee loading accounting for muscle activity in subjects with KOA.

The current study has some limitations that should be considered. First, the cross-sectional design, which precludes a causal relationship between co-activation and medial knee load. Longitudinal studies are necessary to answer this issue. Second, our findings are related to patients with predominantly medial KOA and thus, our results should not be generalized to other samples, mainly when the sample is composed of patellofemoral OA subjects. Third, as this is a study on co-activation between muscles around the knee, the medial hamstring could contribute to understanding this association. However, considering that previous studies found

higher medial and lateral co-activation between the guadriceps and gastrocnemius (Hubley-Kozey, Hill, 2009, Lewek, Rudolph, 2004, Schmitt and Rudolph, 2007), we believe that this would not change the current result. Fourth, we did not measure laxity in our participants, which may have influenced our findings given that a previous study (Lewek, Rudolph, 2004) found greater medial co-activation (VM:MG) in KOA subjects with medial laxity. However, we do not believe that laxity influenced our results because Lewek's study pointed out that nine out of twelve subjects reported instability symptoms, while none of our subjects reported these symptoms. Fifth, it is well established that walking speed is an important variable and should be controlled during gait evaluations (Astephen Wilson, 2012). Although we did not monitor the walking speed, we believe that this limitation did not affect our findings as the included trials showed small variability (less than 5% of the average) within trials. Sixth, we measured the lower limb alignment using the anteroposterior knee radiograph, which is not the gold standard method (Felson et al., 2009), however it presents good reproducibility and demonstrated high correlation with the gold standard method (r= 0.87 - 0.92). Finally, our sample was not matched for BMI, which is also a limitation. To minimize the influence of BMI, the external knee moments were normalized by the height and body weight, which is appropriate to remove the effect of these variables (Moisio et al., 2003). In this context, future studies should investigate the relationship between co-activations, knee moments, and cartilage loss. In addition, intervention programs should investigate the effects on co-activation measures.

5. Conclusion

In conclusion, although KOA showed higher medial knee load compartment, no differences between groups were found for muscle co-activation (ratios and sums). Despite this, there was a correlation only in the KOA group of specific coactivation ratios (VL:BF and QUA:GAST) and sums (VM:MG, EXT:FLX, and QUA:GAST) with external knee adduction moments. These co-activations would cooperate to develop a more comprehensive approach to knee loading in subjects with KOA, accounting not only for external moments but also for muscle activity.

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Figure 1. Bar graph showing the group mean and standard error of knee adduction angular impulse (KAAI) (%Bw*Ht*s), knee flexion moment (KFM) (%Bw*Ht), first, and second external knee adduction moment (EKAM) (%Bw*Ht). Independent t test (α =0.05). *Significantly different from control group (p<0.05).

Figure 2. Bar graph showing the group mean and standard error of co-activation ratios and sums during the stance phase. VL: vastus lateralis, BF: biceps femoris, LG: lateral gastrocnemius, VM: vastus medialis, MG: medial gastrocnemius, EXT: extensors (VM, VL and rectus femoris), FLX: flexors (BF, MG and LG), QUA: quadriceps (VM and VL), GAST: gastrocnemius (MG and LG). Mann-Whitney U test (α =0.05)

Figure 3. Bar graph showing the group mean and standard error of co-activation ratios and sums during the early stance phase (0 – 32%). VL: vastus lateralis, BF: biceps femoris, LG: lateral gastrocnemius, VM: vastus medialis, MG: medial gastrocnemius, EXT: extensors (VM, VL and rectus femoris), FLX: flexors (BF, MG and LG), QUA: quadriceps (VM and VL), GAST: gastrocnemius (MG and LG). Mann-Whitney U test (α =0.05)







Variable	Control Group	KOA Group	
	(n= 19)	(n= 25)	P value
	Mean (SD)	Mean (SD)	
Male:Female	11:8	12:13	
Age (years)	56.6 (5.0)	57.3 (5.3)	0.666
Height (m)	1.66 (0.10)	1.67 (0.09)	0.811
Body Mass (kg)	70.5 (14.6)	79.1 (14.9)	0.063
BMI (kg/m²)	25.2 (3.3)	28.2 (4.0)	0.011*
Gait Speed (m/s)	1.24 (0.15)	1.19 (0.15)	0.227
Lower Limb Alignment (°)	179.1 (2.3)	177.6 (2.2)	0.03*
WOMAC Total Score	1.7 (2.8)	35.8 (19.1)	<0.001*
WOMAC Pain Score	O (O)	7.6 (3.9)	<0.001*
WOMAC Stiffness Score	0.1 (0.2)	3.2 (1.9)	<0.001*
WOMAC Physical Function Score	1.6 (2.7)	25 (14.2)	<0.001*

Table 1. Demographic characteristics

SD: standard deviation, m: meters, Kg: kilograms, m²: square meters, s: seconds, (°): degrees, WOMAC: Western Ontario & McMaster Universities Osteoarthritis Index. The varus lower limb alignment was defined as angles < 180°.

*Significantly different from control group (p<0.05).

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		V	L:BF	VL:LG		VM:MG		EXT:FLX		QUA:GAST	
		KOA	Control	КОА	Control	KOA	Control	КОА	Control	КОА	Control
Co-activation ratios	KAAI	70*	.39	15	11	12	.11	.03	.13	41*	.05
	KFM	.16	18	.21	.13	<.01	<.01	10	10	0.02	08
	1 st EKAM	74*	.12	19	20	.06	.25	.20	.14	28	.31
	2 nd EKAM	53*	.30	36	07	24	.16	.07	.16	53*	.07
Co-activation sums	KAAI	.39	.40	25	.24	42*	.50*	37	.29	47*	.27
	KFM	04	19	.12	11	.05	31	02	22	06	27
	1 st EKAM	.41	.22	30	.22	47*	.36	49*	.18	55*	.15
	2 ^{na} EKAM	.38	.26	19	.22	50*	.50*	40	.25	51*	.23

Table 2. Correlation between co-activation (ratios and sums) and knee moments (KAAI, KFM, first, and second EKAM) of KOA and control groups during the stance phase.

KOA: knee osteoarthritis, VL: vastus lateralis, BF: biceps femoris, LG: lateral gastrocnemius, VM: vastus medialis, MG: medial gastrocnemius, EXT: extensors, FLX: flexors, QUA: quadriceps, GAST: gastrocnemius, KAAI: knee adduction angular impulse (%Bw*Ht*s), KFM: knee flexion moment (%Bw*Ht), 1st EKAM: first external knee adduction moment (%Bw*Ht), 2nd EKAM: second external knee adduction moment (%Bw*Ht).

Spearman rank test between variables.

*Significant correlation (p≤0.05)

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		V	L:BF	VL:LG		VM:MG		EXT:FLX		QUA:GAST	
		KOA	Control	КОА	Control	KOA	Control	KOA	Control	КОА	Control
Co-activation ratios	KAAI	21	.47	17	.24	.05	.07	<.01	.08	.14	.34
	KFM	02	29	10	<.01	.09	22	49*	.25	12	<.01
	1 st EKAM	22	.45	26	.19	14	12	18	.04	<.01	.11
	2 nd EKAM	36	.41	30	.23	.23	<.01	11	.11	.03	.37
Co-activation sums	KAAI	.33	.46	05	.22	07	.36	06	.13	07	.19
	KFM	.15	11	.26	02	.07	32	.09	18	.11	20
	1 st EKAM	.31	.33	.01	.22	13	.27	18	.15	07	.18
	2 ¹¹⁰ EKAM	.24	.36	.05	.14	<.01	.29	17	.06	<.01	.12

Table 3. Correlation between co-activation (ratios and sums) and knee moments (KAAI, KFM, first, and second EKAM) of KOA and control groups during early stance phase (0 - 32%).

KOA: knee osteoarthritis, VL: vastus lateralis, BF: biceps femoris, LG: lateral gastrocnemius, VM: vastus medialis, MG: medial gastrocnemius, EXT: extensors, FLX: flexors, QUA: quadriceps, GAST: gastrocnemius, KAAI: knee adduction angular impulse (%Bw*Ht*s), KFM: knee flexion moment (%Bw*Ht), 1st EKAM: first external knee adduction moment (%Bw*Ht), 2nd EKAM: second external knee adduction moment (%Bw*Ht).

Spearman rank test between variables.

*Significant correlation (p≤0.05)

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