



Original Article

The Comparison of Knee Joint Muscle Flexibility between Women with and without Radiographic Knee Osteoarthritis

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ABSTRACT

Background: Approximately 60% of individuals above 50 years of age are affected by knee osteoarthritis (KOA). KOA is most commonly assessed through radiographic evaluation and classified using the Kellgren -Lawrence (KL) grading system with KL Grade 0 (KLG0) indicating a definite absence of radiographic KOA (RKO) and KLG2 presenting a definite presence of RKO. The current study compared knee joint muscle flexibility among three groups with KLG0, KLG2, and KLG3 RKO.

Methods: In this descriptive cross-sectional study, 94 KLG0, KLG2, and KLG3 knees on 57 women aged ≥ 40 years were examined. The flexibility of the quadriceps, hamstring, iliotibial band, adductor, and gastrocnemius muscles was compared.

Results: Iliotibial band flexibility was lower in subjects with KLG3 RKO than those with KLG2 ($P < 0.05$) or KLG0 ($P \leq 0.001$) RKO, with the latter two groups being statistically equivalent ($P = 0.075$). In addition, quadriceps muscle flexibility was lower in subjects with KLG3 RKO than those with KLG2 ($P \leq 0.001$) or KLG0 ($P \leq 0.001$) RKO, with the latter two groups being statistically different ($P \leq 0.001$). No significant differences were found between groups regarding other muscles ($P > 0.05$).

Conclusion: In patients with RKO, the flexibility of the iliotibial band and quadriceps muscles may decrease as the disease progresses from KLG2 to KLG3. Moreover, quadriceps and iliotibial band flexibility may be lower in KLG3 compared to KLG0, with a lower likelihood of quadriceps flexibility in KLG2 compared to KLG0. These results suggest that quadriceps and iliotibial band stretching may be potentially important components of treatment.

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Introduction

Musculoskeletal disorders are one of the main causes of disability [1], with knee symptoms ranked second in prevalence [2]. KOA is the most common cause of knee symptoms in older adults [3], and its prevalence increases with age. Higher rates of KOA are seen among women

than in men [4-6]. Approximately 60% of individuals above the age of 50 years are affected by KOA [7]. The osteoarthritis (OA) burden has risen over recent decades [8] and will continue to rise in developed and developing countries which have rapidly growing elderly populations [1, 9]. OA, as the 11th highest contributor to global disability in the elderly [10], leads to functional limitations in daily activities such as walking and climbing stairs [11-13]. It has also been predicted to be the fourth leading cause of disability in the coming 20 years [3, 14]. Because of the high prevalence of OA and

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its effect on functional abilities, the need to identify the factors influencing this severe condition is clear [15].†

From the pathogenesis perspective, OA risk factors are divided into systemic and local factors. While systemic factors involve multiple joints (generalized OA), they tend to be biochemical and lead to joint damage or impairment of the joint repair process. Local or mechanical factors involving a special single joint also tend to be biomechanical and are linked to the forces encountered at the joint [16]. Systemic parameters include factors such as age, gender, genetics, ethnicity, biochemical markers of cartilage or bone metabolism, and obesity (metabolic alterations) [17]. Local factors are, in turn, classified as intrinsic or extrinsic to the joint. Local intrinsic factors have an origin internal to the joint and consist of factors such as alignment, laxity, proprioception, range of motion (ROM), and strength [18]. Conversely, local extrinsic factors like injury, sports participation, and obesity (increased load) arise from the events occurring external to the joint [19].

In addition, OA risk factors can be classified as modifiable and nonmodifiable. Although many of the aforementioned risk factors like age, gender, genetics, and ethnicity are fixed, other factors such as obesity, sports participation, strength, and ROM are modifiable [20, 21]. Although modifiable risk factors may have an essential role to prevent disease onset and progression, only a few of them have been the focus of attention. There is a paucity of literature that have explored the ROM of the knee.

Of note, decreased ROM at the knee may change forces applied to the joint. For instance, when a knee cannot fully extend during gait, the tibiofemoral joint contact area is minimized and more pressure is applied over a smaller joint surface [22]. This greater force may, in turn, lead to cartilage erosion [18]. Some studies have shown that flexion extension ROM of the knee may decrease in individuals with KOA [23-25]. This decreased flexion extension at the knee as well as tibial lateral and medial rotation decline may be related to KOA severity [23].

On the other hand, the amount of joint mobility or ROM is dependent on the muscle length as soft tissue and bony structures in the area [26]. Thus, a patient with impaired flexibility also has a limited range of motion. Nevertheless, few studies have investigated knee joint muscle flexibility in individuals with KOA. Decreased quadriceps [27, 28], hamstring [27, 29, 30], iliotibial band, adductors, and gastrocnemius flexibility [27] is reported in patients with KOA compared to healthy people. In addition, differences in knee joint muscle flexibility among different stages of the disease have not been investigated.

From the pathologic perspective, OA might be characterized as localized cartilage erosion extending to the bone underneath the cartilage with osteophytes, joint space loss, sclerosis, and cysts appearing in radiographic views [17]. Radiographic evaluation of OA, as the best method of imaging the biologic status of a joint, is used in most epidemiologic studies [31]. RKOA is mainly assessed by the KL grading scale [32, 33]. This system is the gold standard [34] of radiological classification for

identifying and grading the severity of tibiofemoral KOA [35] with five global grades (0-4) [36]. KLG0 indicates a definite absence of RKOA, and KLG2 is used as a cut-off for a definite presence of RKOA [35]. The presence or absence of the disease diagnosed by radiographic findings demonstrates a strong dissociation with clinical symptoms. One study reported that 60% of patients with moderate RKOA and 40% of those with severe RKOA have no symptoms [37]. Thus, many people with RKOA may have no symptoms [17] but cannot be considered as a healthy control. Studies comparing knee joint muscle flexibility between KOA patients and asymptomatic controls have considered asymptomatic subjects as healthy controls.

Modifiable local intrinsic risk factors play an essential role in prevention strategies for controlling KOA incidence and progression. One of these modifiable local intrinsic risk factors may be the flexibility of knee joint muscles. Despite the evidence demonstrating strong dissociations between clinical symptoms and radiographic data in osteoarthritic knees, few studies investigating flexibility variables in these patients have compared the flexibility of knee joint muscles between subjects with RKOA and asymptomatic individuals considered as non-osteoarthritic knees. Moreover, knee joint muscle flexibility in different stages of RKOA have not been compared. The data suggests the existence of a clear need to study differences in knee joint muscle flexibility in subjects with and without RKOA as well as the differences between various stages of the disease. The current study compared the flexibility of the muscles around the knee joint in three groups of women with KLG0, KLG2, and KLG3 RKOA in order to determine whether there is a difference between women with mild (KLG2) and those with moderate (KLG3) RKOA in terms of knee joint muscle flexibility as well as the differences between those with and those without RKOA.

Methods

Ninety-four knees of 57 women with an age of ≥ 40 years, body mass index BMI ≤ 30 , and tibiofemoral KL radiographic scores of 0, 2, and 3 were enrolled in this descriptive cross-sectional study [4, 35, 36, 38-40]. All patients were referred to a single radiology center over a one-year period and had bilateral anteroposterior knee radiographs obtained in weight-bearing, full extension standardized manner. KLG1 has not been included, because Dieppe [36] stated that mild KOA (KLG2) characterizes the new development of OA, and this state should not yet be considered a disease, because, it does not progress for a long time. Those with a history of non-recreational or professional athletic training, knee joint trauma or surgery, loss of knee joint play, rheumatoid or other inflammatory arthritis, joint infection, neuropathic arthropathy [28, 41], generalized OA, and those with end-stage disease defined as KLG4 were excluded from the study. Subjects with KLG4 were excluded, because they usually cannot walk independently on a flat surface without an ambulatory assistive device. Approval was given by the Ethical Review Committee of Tehran

University. Written informed consent was obtained from each subject prior to study participation.

Data on the age, weight, and height of the subjects was collected, and body mass index was calculated for each participant (weight/height²).

Radiographic Scoring

Based on the KL grading scale [32, 33], radiographs were scored by a single investigator (HM) blinded to the flexibility data at the time of examination. Readings were made after holding 100 hours of training and 5 training sessions each of 2 hours duration under the supervision of an experienced orthopedic surgeon. To assess intra-rater reliability, 22 radiographs were randomly chosen, and reading was repeated one week later without knowledge of the previous results. While KLG0 indicated a definite absence of RKOA, KLG2 was chosen as a cut-off point for minimal or mild RKOA and KLG3 determined to indicate moderate RKOA [35].

Clinical Examination

All flexibility measurements were performed by the same examiner (HM) using universal 360 degree goniometers constructed of clear, flexible plastic and a digital inclinometer (INSIZE model 2170-1 electronic level and a protractor, 4×90°). Prior to any measurement, the accuracy of the instruments was validated against 0, 45, 90, 135, and 180 degrees [42]. All flexibility tests were performed two times with a 10-s rest between efforts. The average of two trials was recorded to the nearest 1° for all muscle tests [43]. The reliability of the flexibility measurements used in this study has been previously examined and considered good to excellent [43-46]. However, considering variations in measurement methodology, devices used (e.g., digital inclinometer against gravity inclinometer), differences between studied populations, and even the interpretation of correlation coefficients, the intra-rater reliability for all flexibility measurements was determined. Reliability studies were performed on 22 limbs using a double session (measurements taken twice each session), repeated measures design, and one examiner.

Hamstring flexibility was measured using a passive knee extension test. With the subject in supine position, the opposite knee was placed at 90° of flexion with the shank off the plinth and the hip extended. The limb to be measured had the pelvis immobilized, the hip maintained at 90° of flexion, and its ankle relaxed in plantarflexion. In this position, the examiner passively extended the knee until resistance was felt. While an assistant held the position, the examiner placed the center of the goniometer on the femoral condyle and aligned the stationary arm with the shaft of the femur. Then the distal arm was placed parallel to the tibia. The angle was recorded in degrees [46].

Quadriceps flexibility was measured with subjects in the prone position. Measurement was made with the use of the digital inclinometer zeroed on a horizontal surface prior to the measurements. The examiner flexed the patient's knee passively to the point where the lumbar spine began to extend or the pelvis tilted toward the

anterior. Then the digital inclinometer was placed over the anterior distal tibia [45], and the angle between the distal tibia and the vertical was recorded in degrees. A positive score indicated that the lower leg reached past the vertical, while a negative score indicated that the lower leg did not reach the vertical.

Adductors flexibility was measured with patient in the supine position and the non-test hip in 10° of abduction. To maintain the non-test hip in abduction, the pelvis was stabilized, allowing full ROM in the test-hip [47]. The fulcrum of the goniometer was positioned on the anterior superior iliac spine (ASIS) of the test-side, and the stationary arm was placed on the opposite ASIS. While the participant maintained the stationary arm of the goniometer, the examiner aligned the moving arm with the midline of the test-thigh and abducted the test-leg while supporting its calf and foot until firm resistance was felt. The obtuse angle was subtracted by 90° and the result was recorded as the adductor flexibility [43].

Iliotibial band flexibility was measured with the subject lying on his/her side and using Ober's test. To aid standardization, the lower hip and knee were positioned in 90° of flexion. The examiner grasped the test leg just below the knee. The knee was flexed 90° and the hip was brought from flexion/abduction to the neutral extension with the hip in neutral rotation. From this position, the thigh was allowed to drop toward the table. The endpoint was achieved when the pelvis began to tilt laterally. At that point, the inclinometer was positioned over the lateral portion of the distal femur and the angle was recorded. The digital inclinometer was zeroed on a horizontal surface prior to measurement. The angle was expressed as negative if the thigh endpoint was above horizontal, positive if the thigh endpoint reached below horizontal, and zero if the limb was horizontal [44, 45, 48].

Gastrocnemius flexibility was measured with the patient in the prone position. The participant was asked to extend the knee and let the foot hang off the table. With the subtalar joint in the neutral position, the examiner brought the ankle to dorsiflexion. When resistance was felt, the examiner placed the fulcrum of the goniometer on the lateral malleolus and aligned the stationary arm with the lateral midline of the leg while positioning the moving arm on the lateral midline of the foot [45]. The angle was recorded in degrees.

Data Analysis

SPSS version 24 was used for all analyses. Intra-rater reliability for flexibility measurements was examined with the intra-class correlation coefficient, and measurements of intra-rater reliability for ordinal variables were evaluated using a weighted kappa coefficient. Descriptive statistics were conducted for all demographic characteristics and flexibility measures. All variables demonstrated normal distribution when examined using the Shapiro-Wilk test. Differences between subjects with KLG0, KLG2, and KLG3 were evaluated using analysis of variance (ANOVA) with a Gabriell post hoc test because of the homogeneity of all flexibility variables. All tests were performed with a level of significance of 0.05 (two-tailed).

Table 1: Baseline characteristics of the study participants

Variables	KLG0 n=27	KLG2 (n=38)	KLG3 (n=29)
Age	53.96±11.53	59.42±12.52	63.71±9.08
Weight	62.36±7.43	66.97±8.27	71.15±7.09
Height	159.40±4.99	157.55±5.94	157.13±5.73
BMI	24.57±2.65	26.92±2.35	28.77±1.91

Notes. Values are expressed as mean±standard deviation; KLG=Kellgren Lawrence grade; BMI=body mass index; age in years, weight in kilograms, height in meters, and BMI in Kg/m².

Table 2: Differences in muscle flexibility between subjects with and without Radiographic Knee Osteoarthritis (RKO)

Variables	KLG0 (n=27)	KLG2 (n=38)	KLG3 (n=29)	F(2,91)	P
Quadriceps	35.29±16.13*	17.46±13.41	10.29±15.63 [^]	15.272	<0.001
Hamstring	44.56±7.75	43.54±8.53	44.04±12.43	0.31	0.970
Iliotibial band	-6.42±5.80	-10.30±6.02 ^l	-13.10±6.00 [^]	10.273	<0.001
Adductor	28.82±5.23	27.23±6.23	26.98±5.14	0.847	0.432
Gastrocnemius	19.36±6.14	20.05±6.49	18.33±6.30	0.813	0.447

Values are expressed as mean±standard deviation; KLG=Kellgren Lawrence grade; * significant difference between KLG0 and KLG2 (P≤0.001); [^] significant difference between KLG0 and KLG3 (P≤0.001); ^l significant difference between KLG2 and KLG3 (P<0.05); ^{||} significant difference between KLG2 and KLG3 (P≤0.001).

Results

Ninety-four knees of 57 women with a mean age of 59.24±11.83 years (range=40 to 86 year) and mean BMI of 26.84±2.82 Kg/m² were evaluated in the present study. Subjects were divided into three groups: KLG0 (n=27), KLG2 (n=38), and KLG3 (n=29). The demographic data of each group is presented in Table 1.

In terms of reliability, the KL grading scale showed a high value for intra-rater reliability with a kappa coefficient $\kappa=0.88$ [49]. The flexibility measurements demonstrated excellent intra-rater reliability with ICCs ranging from 0.84 to 0.98 [49].

ANOVA results found no difference between subgroups for hamstring, adductor, and gastrocnemius flexibility, but quadriceps and iliotibial band flexibility was found to be different between groups. Thus, post hoc analysis was made to determine which groups statistically differed for the two parameters. Results of the Gabrielle test revealed that iliotibial band flexibility was significantly lower in subjects with KLG3 RKOA -13.10±6.00 than in those with KLG2 RKOA -10.30±6.02 (P<0.05) and those with KLG0 RKOA -6.42±5.80 (P≤0.001), with the latter two groups being statistically equivalent (P=0.075). Moreover, the mean quadriceps muscles flexibility was lower in the KLG3 RKOA group (10.29±15.63) than in the KLG2 RKOA (17.46±13.41; P≤0.001) and KLG0 RKOA groups (35.29±16.13; P≤0.001), with the latter two groups being statistically different (P≤0.001). Table 2 presents a detailed overview of the findings.

Discussion

The aim of this study was twofold: First, to determine the difference in knee joint muscle flexibility between women with KLG2 (mild) and KLG3 (moderate) RKO, and second, to investigate whether there is a difference between women with and without RKO.

The findings did not demonstrate a significant difference in hamstring, adductors, or gastrocnemius muscle flexibility between mild and moderate RKO groups, however, significant differences were found in

the flexibility of quadriceps and iliotibial band between these two groups (P≤0.001, P≤0.05, respectively). Few studies were found to have assessed knee joint muscle flexibility in patients with different grades of RKO. Therefore, there are no head-to-head studies with which to compare the results. Because poor flexibility is a major cause of joint dysfunction [50], the results of the present study may be considered as evidence consistent with population-based longitudinal studies that have revealed the association of RKO progression as measured by KL grade with physical function decline [13, 51-54]. Taking into account the association between disease progression and function reduction as well as the effect of poor flexibility in joint dysfunction, it can be concluded that disease severity may have an association with knee joint muscle flexibility. Thus, the current study investigated the difference in knee joint muscle flexibility between subjects with mild and moderate RKO. Significant lower quadriceps and iliotibial band flexibility was found in those with KLG3 RKO compared with those who had KLG2 RKO. These results may be considered as evidence confirming the association between disease severity and knee joint muscle flexibility that could be considered a therapeutic target.

To the best of the authors' knowledge, few studies have documented the differences in knee joint muscle flexibility between subjects with and without KOA. Two studies investigated quadriceps muscle flexibility and reported lower quadriceps length in patients with KOA compared to healthy controls [27, 28]. The current results were consistent with these studies for both mild and moderate RKO, suggesting the role of the quadriceps muscle in knee function.

One earlier study reported decreased iliotibial band flexibility in subjects with KOA (disease severity not mentioned) compared to healthy individuals [27]. However, another study noted no significant iliotibial band length difference between grades 2 and 3 KOA (included in 1 group) and healthy controls [28]. After separating KLG2 patients from those with KLG3 RKO, the current study found lower iliotibial band flexibility

in subjects with KLG3 compared to those with KLG0, but iliotibial band length was equivalent in the KLG0 and KLG2 groups ($P=0.075$). This data suggests that the distinction between different grades of the disease may better reveal the differences between knees with and without OA.

No difference was observed in hamstring, adductors, or gastrocnemius muscle flexibility between the female groups in the current study. These results were consistent with another study that examined female participants [28], but contrary to the results of previous studies that included both males and females in terms of hamstring [27, 29, 30], adductors [27], and gastrocnemius [27] muscle lengths.

We believe these discrepancies may first be attributed to the gender difference between these studies. Nagaosa et al. [55] noted different mean widths in the tibiofemoral joint between men and women. Given the importance of joint space narrowing as one of the two major cardinal features of RKO, joint space width difference between men and women may affect the results. In addition, BMI was not controlled in any of those studies. The lack of weight control in epidemiologic studies may increase the systemic and mechanical effects of weight on joint tissue damage [56], confounding the outcomes. Moreover, differences in participant characteristics such as age may affect the results [39]. These variations make it difficult for such data to be properly compared.

As mentioned before, many people with RKO have no symptoms. Healthy case selection in previous studies investigating differences in knee joint muscle flexibility between healthy and osteoarthritic knees has relied on symptom definition. Moreover, differences in flexibility factors in various stages of the disease had not been previously investigated. Furthermore, many studies have found RKO severity to be a baseline risk factor for functional decline in older adults, while OA is one of the highest contributors to global disability, with the highest OA burden being attributed to hip and KOA. Therefore, the urgent need to conduct studies with the focus on modifiable risk factors of the disease such as flexibility parameters is highlighted. This research was the first to investigate knee joint muscle flexibility differences between subjects with and without RKO as well as between those with mild and moderate RKO. These findings, based on quadriceps and iliotibial band length differences among our three groups of KLG0, KLG2, and KLG3, may have implications for disease incidence and progression prevention.

This study had several limitations. First, its participants were women, so the results cannot be generalized to male patients. Further research on groups of males is recommended. Second, the measurements in this study were made and recorded by the same examiners, neither of whom was blinded. Third, the study population comprised symptomatic patients who had been referred to a radiology center because of knee pain. Thus, another study with a symptom-free population without RKO included as the control group may better detect differences between patients with and without RKO.

Conclusion

Quadriceps and iliotibial band lengths were found to be reduced in women with moderate RKO compared to those with mild RKO. Also, lower quadriceps and iliotibial band flexibility was found in subjects with moderate RKO compared to non-RKO subjects. Quadriceps flexibility also showed a decreased value in subjects with mild RKO compared to non-RKO subjects. Quadriceps and iliotibial band tightness can be useful targets in developing interventions to treat or prevent KOA.

Conflict of Interest: None declared.

References

- Brooks P.M. The burden of musculoskeletal disease-a global perspective. *Clin Rheumatol*. 2006;25(6):778-781.
- Belo JN, Bierma-Zeinstra S, Raaijmakers AJ, Van der Wissel F, Opstelten W. The Dutch College of General Practitioners (NHG) Practice Guideline for nontraumatic knee problems in adults (first revision) [NHG-Standaard niet-traumatische knieproblemen bij volwassenen (Dutch title)]. *Huisarts en Wetenschap*. 2008;51:229-240.
- Belo J. Nontraumatic knee complaints in adults in general practice. Erasmus Medical Center, Rotterdam, The Netherlands. 2009. [PhD thesis].
- Andrianakos AA, Kontelis LK, Karamitsos DG, Aslanidis SI, Georgountzos AI, Kaziolas GO, et al. Prevalence of symptomatic knee, hand, and hip osteoarthritis in Greece. The ESORDIG study. *J Rheumatol*. 2006;33(12):2507-2513.
- Cooper C, Dennison E, Edwards MH, Litwic A. Epidemiology of osteoarthritis. *Medicographia*. 2013;35(2):145-151.
- Jordan JM, Helmick CG, Renner JB, Luta G, Dragomir AD, Woodard J, et al. Prevalence of knee symptoms and radiographic and symptomatic knee osteoarthritis in African Americans and Caucasians: the Johnston County Osteoarthritis Project. *J Rheumatol* 2007;34(1):172-180.
- Carvalho NA, Bittar ST, Pinto FR, Ferreira M, Sitta RR. Manual for guided home exercises for osteoarthritis of the knee. *Clinics*. 2010;65(8):775-780.
- March LM, Bachmeier CJ. Economics of osteoarthritis: a global perspective. *Baillieres Clin Rheumatol* 1997;11(4):817-834.
- El-Tawil S, Arendt E, Parker D. Position statement: the epidemiology, pathogenesis and risk factors of osteoarthritis of the knee. *J ISAKOS*. 2016;1(4):219-228.
- Cross M, Smith E, Hoy D, Nolte S, Ackerman I, Fransen M, et al. The global burden of hip and knee osteoarthritis: estimates from the global burden of disease 2010 study. *Ann Rheum Dis*. 2014;73(7):1323-1330.
- Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health*. 1994;84(3):351-358.
- Murray CJ, Richards MA, Newton JN, Fenton KA, Anderson HR, Atkinson C, et al. UK health performance: findings of the Global Burden of Disease Study 2010. *Lancet*. 2013;381(9871):997-1020.
- White DK, Neogi T, Nguyen UN, Niu J, Zhang Y. Trajectories of functional decline in knee osteoarthritis: the Osteoarthritis Initiative. *Rheumatology (Oxford)*. 2016;55(5):801-808.
- Woolf AD, Pfleger B. Burden of major musculoskeletal conditions. *Bull World Health Organ*. 2003;81(9):646-656.
- Johnsen MB, Hellevik AI, Baste V, Furnes O, Langhammer A, Flugsrud G, et al. Leisure time physical activity and the risk of hip or knee replacement due to primary osteoarthritis: a population based cohort study (The HUNT Study). *BMC Musculoskelet Disord*. 2016;17(2):86-96.
- Nwosu LN. Structural and pain modifications in models of osteoarthritis. University of Nottingham. 2015. [PhD thesis]
- Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. *Ann Intern Med*. 2000;133(8):635-646.

18. Gibson K. Pain and function in knee osteoarthritis: are they related to local intrinsic factor? University of Missouri. 2008. [PhD Thesis]
19. Sharma L. Local factors in osteoarthritis. *Curr Opin Rheumatol*. 2001;13(5):441-446.
20. Jackson BD, Wluka AE, Teichtahl AJ, Morris ME, Cicuttini FM. Reviewing knee osteoarthritis—a biomechanical perspective. *J Sci Med Sport*. 2004;7(3):347-357.
21. Johnson VL, Hunter DJ. The epidemiology of osteoarthritis. *Best Pract Res Clin Rheumatol*. 2014;28(1):5-15.
22. Hertling D, Kessler RM. Management of common musculoskeletal disorders: Physical therapy principles and methods (4th ed). Philadelphia: Lippincott Williams and Wilkins. 2006.
23. Ersoz M, Ergun S. Relationship between knee range of motion and Kellgren-Lawrence radiographic scores in knee osteoarthritis. *Am J Phys Med Rehabil*. 2003;82(2):110-115
24. Fishkin Z, Miller D, Ritter C, Ziv I. Changes in human knee ligament stiffness secondary to osteoarthritis. *J Orthop Res*. 2002;20(2):204-207.
25. Messier SP, Loeser RF, Hoover JL, Semble EL, Wise CM. Osteoarthritis of the knee: effects on gait, strength, and flexibility. *Arch Phys Med Rehabil*. 1992;73(1):29-36.
26. Houglum PA. Therapeutic exercise for athletic injuries. Human kinetics. 2001.
27. Jyoti SJ, Yadav V S. Knee Joint Muscle Flexibility in Knee Osteoarthritis Patients and Healthy Individuals. *Int J Health Sci Res*. 2019;9(6):156-163.
28. Shirazi SA, Nezhad FG, Ebrahimian M, Nouraddini E, Mansoorian A, Emami F. Flexibility of Knee Joint Muscles in Women with Knee Osteoarthritis and Healthy Controls. *J Rehabil Sci Res*. 2015;2(3):47-52.
29. Fernando W, Wettasinghe AH, Dissanayake WDD. Comparison of hamstring muscle length between patients with osteoarthritis of knee and without osteoarthritis of knee. *Peradeniya Uni International Research Sessions*. 2014;18(7):243.
30. Onigbinde AT, Akindoyi O, Faremi FA, Okonji A, Shuaib O, Lanre OO. An assessment of hamstring flexibility of subjects with knee osteoarthritis and their age matched control. *Clinical Medicine Research*. 2013;2(6):121-125.
31. Felson DT, Zhang Y. An update on the epidemiology of knee and hip osteoarthritis with a view to prevention. *Arthritis Rheum*. 1998;41(8):1343-1355.
32. Empire Rheumatism Council. The epidemiology of chronic rheumatism. Atlas of standard radiographs of arthritis. Oxford: Blackwell Scientific Publications 1963.
33. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis*. 1957;16:494-502.
34. Hart DJ, Spector TD. The classification and assessment of osteoarthritis. *Baillieres Clin Rheumatol*. 1995;9(2):407-432.
35. Schiphof D, Boers M, Bierma-Zeinstra SM. Differences in descriptions of Kellgren and Lawrence grades of knee osteoarthritis. *Ann Rheum Dis*. 2008;67(7):1034-1036.
36. Dieppe P. Theories on the pathogenesis of OA. Presented at: Stepping Away From OA: A Scientific Conference on the Prevention of Onset, Progression, and Disability of Osteoarthritis. 1999;23-24. Bethesda, Md.
37. Anderson JJ, Felson DT. Factors associated with osteoarthritis of the knee in the first national Health and Nutrition Examination Survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *Am J Epidemiol*. 1988;128(1):179-189.
38. Jiang L, Tian W, Wang Y, Rong J, Bao C, Liu Y, et al. Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. *Joint Bone Spine*. 2012;79(3):291-297.
39. Palazzo C, Nguyen C, Lefevre-Colau MM, Rannou F, Poiraudou S. Risk factors and burden of osteoarthritis. *Ann Phys Rehabil Med*. 2016;59(3):134-138.
40. Silverwood V, Blagojevic-Bucknall M, Jinks C, Jordan JL, Protheroe J, Jordan KP. Current evidence on risk factors for knee osteoarthritis in older adults: a systematic review and meta-analysis. *Osteoarthritis Cartilage*. 2015;23(4):507-515.
41. Sharma L, Song J, Felson DT, Cahue S, Shamiyeh E, Dunlop DD. The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *Jama*. 2001;286(2):188-195.
42. Boone DC, Azen SP, Lin CM, Spence C, Baron C, Lee L. Reliability of goniometric measurements. *Phys Ther*. 1978;58(11):1355-1360.
43. Pua YH, Wrigley TV, Cowan SM, Bennell KL. Intrarater test-retest reliability of hip range of motion and hip muscle strength measurements in persons with hip osteoarthritis. *Arch Phys Med Rehabil*. 2008;89(6):1146-1154.
44. Ferber R, Kendall KD, McElroy L. Normative and Critical Criteria for Iliotibial Band and Iliopsoas Muscle Flexibility. *J Athl Train*. 2010;45(4):344-348.
45. Piva SR, Fitzgerald K, Irrgang JJ, Jones S, Hando BR, Browder DA, et al. Reliability of measures of impairments associated with patellofemoral pain syndrome. *BMC Musculoskelet Disord*. 2006;7(3):33-49.
46. White LC, Dolphin P, Dixon J. Hamstring length in patellofemoral pain syndrome. *Physiotherapy*. 2009;95(1):24-28.
47. Clarkson HM. Musculoskeletal assessment: Joint Motion and Muscle Testing Third Edition. Wolters Kluwer/ Lippincott Williams and Wilkins. 2013.
48. Puniello MS1. Iliotibial band tightness and medial patellar glide in patients with patellofemoral dysfunction. *J Orthop Sports Phys Ther*. 1993;17(3):144-148.
49. Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics*. 1977;33:159-174.
50. Page P, Frank C, Lardner R. Assessment and treatment of muscle imbalance: the Janda approach: *Human Kinetics*; 2010:43-44.
51. Holla JF, van der Leeden M, Heymans MW, Roorda LD, Bierma-Zeinstra SM, Boers M, et al. Three trajectories of activity limitations in early symptomatic knee osteoarthritis: a 5-year follow-up study. *Ann Rheum Dis*. 2014;73(7):1369-1375.
52. Riddle DL, Stratford PW. Body weight changes and corresponding changes in pain and function in persons with symptomatic knee osteoarthritis: a cohort study. *Arthritis Care Res*. 2013;65(1):15-22.
53. Sharma L, Cahue S, Song J, Hayes K, Pai YC, Dunlop D. Physical functioning over three years in knee osteoarthritis: role of psychosocial, local mechanical, and neuromuscular factors. *Arthritis Rheum*. 2003;48(12):3359-3370.
54. Wesseling J, Bierma-Zeinstra SM, Kloppenburg M, Meijer R, Bijlsma JW. Worsening of pain and function over 5 years in individuals with 'early' OA is related to structural damage: data from the Osteoarthritis Initiative and CHECK (Cohort Hip and Cohort Knee) study. *Ann Rheum Dis* 2015;74(2):347-353.
55. Nagaosa Y, Mateus M, Hassan B, Lanyon P, Doherty M. Development of a logically devised line drawing atlas for grading of knee osteoarthritis. *Ann Rheum Dis*. 2000;59(8):587-595.
56. Sharma L, Lou C, Cahue S, Dunlop DD. The mechanism of the effect of obesity in knee osteoarthritis: the mediating role of malalignment. *Arthritis Rheum*. 2000;43(3):568-575.