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Research Article

Assessment of Knee Osteoarthritis Severity using New Multifactorial Scale (KHIUS) in Northwest Syria

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Abstract: The present study aimed to identify the risk factors associated with knee osteoarthritis (OA) in Northwest Syria and to evaluate the reliability of our newly proposed Khatib-Khaled Idlib University Scale (KHIUS) in assessing knee OA severity. The study enrolled 101 patients with knee OA, diagnosed through X-ray at the orthopedic clinic. The Kellgren and Lawrence classification was employed to determine the X-ray knee OA grades. The erythrocyte sedimentation rate (ESR) value was obtained as a biomarker after excluding rheumatoid arthritis, other inflammatory diseases, and malignant tumors. The risk factors of knee OA assessed in our study included age, gender, BMI, and physical activity. Each patient completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire and KHIUS to evaluate knee OA severity. Correlation coefficients of two scales, i.e., WOMAC and X-ray knee OA grading as well as KHIUS and X-ray knee OA grading, were determined. The mean age of the patients was 52.84 ± 9.74 years (age range 25-80 years). Most patients had low daily activity levels, and the left knee was the most affected. In our study, the correlation coefficient between WOMAC and KHIUS was strong (R: 80.3%, $P < 0.01$). The correlation coefficient between X-ray KL knee OA grades and WOMAC was moderate (R: 50.9%, $P < 0.01$), whereas the correlation coefficient between X-ray KL knee OA grades and KHIUS was comparatively stronger (R: 75.7%, $P < 0.01$). KHIUS can be a reliable scale to assess knee OA severity and to guide the method of treatment by orthopedic surgeons. In addition, KHIUS is more closely related to X-ray KL knee OA grading than other clinical scales.

Keywords: Knee Osteoarthritis, KHIUS, Risk Factors, ESR, Biomarker, WOMAC.

1. INTRODUCTION

According to the World Health Organization (WHO), Knee Osteoarthritis (KO) is a prevalent condition worldwide. The global incidence rate of this disease is 5% among the adult population over the age of 18 years, with the rate increasing to 10% in males and 14% in females aged between 50 and 69 years old in patients with hip and knee OA [1]. KO is the 4th leading cause of disability in Asia [2], with a confirmed correlation between incidence and income. In high-income regions, there are 358 cases per 100,000 individuals compared to 75 cases per 100,000 individuals in low-income regions. Likewise, in the USA, statistics indicate a disparity in the occurrence of Knee OA between African and White Americans [3]. Studies have shown that a significant number of individuals with radiographically confirmed OA do not experience symptoms. Therefore, the prevalence of radiographic knee OA is believed to be higher than symptomatic knee OA. Knee pain serves as a vague indicator of radiographic knee osteoarthritis, which is somewhat influenced by the extent of radiographic involvement. Similarly, radiographic knee OA provides an uncertain indication of the likelihood of experiencing knee pain or disability. Many individuals with radiographic knee OA do not exhibit symptoms, while conversely, many patients with knee pain suggestive of OA lack radiologic findings. For instance, in South Korea, the prevalence of radiographic knee OA was

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reported to be 21.1% in males and 43.8% in females, while the prevalence of symptomatic knee OA was 4.4% in males and 19.2% in females [4]. Likewise, evidence from a Japanese population-based cohort study indicated a weak association between the symptoms of knee OA and radiographic findings, and vice versa [5]. According to a systematic literature review, 15-76% of individuals with knee pain showed radiographic OA, while 15-81% of those with radiographic knee OA experienced pain [6].

The incidence of OA is strongly associated with aging, as advanced glycation end products accumulate in the cartilage matrix and contribute to cartilage fragility. This process also stimulates the innate immune system in the synovial membrane, leading to the production of pro-inflammatory mediators such as cytokines, which can further contribute to the development and progression of knee OA [7]. In addition, the aging of chondrocytes can lead to a decrease in the production of growth factors such as insulin-like growth factor and transforming growth factor-β, which can further exacerbate knee OA [8]. The incidence of knee OA is higher in females due to the loss of estrogen after menopause, which affects the production of cartilaginous matrix proteins and stimulates the destructive activity of articular cartilage [9]. Obesity is another important factor that triggers OA pathogenesis and contributes to its progression. Obesity has both mechanical effects on weight-bearing joints such as the knee and hip and systemic effects on OA occurrence by releasing adipokines that lead to release of pro-inflammatory cytokines such as IL1β and TNFα, thereby inhibiting the production of collagen II and aggrecan from chondrocytes [10, 11]. However, it is worth to mention that all obese individuals do not develop OA. The most likely explanation for this disparity could be due to other factors such as genetics, joint alignment, and physical activity levels, which may also contribute to the pathogenesis and progression of knee OA. As such, physical activity has shown both positive and negative effects on knee OA, while the atrophy of muscular mass surrounding the knee joint increases the incidence rate of knee OA [12, 13]. Workers in certain occupations such as builders, farmers, firefighters, fishermen, foresters, and miners have also been associated with an increased incidences of knee OA [14]. Various scales are used to assess knee function, including the International Knee Documentation Committee (IKDC), Knee injury and Osteoarthritis Outcome Score (KOOS), Lysholm Knee Scoring Scale, Oxford Knee Score (OKS), and Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) [15-19]. While these scales provide insight into knee OA severity, these rely solely on patient responses to classify the condition. In other words, the current knee assessment criteria used in the above-mentioned scales, including pain severity and joint disability scales, have limitations that affect the accuracy of the assessment due to the fact that these scales depend completely on patient-reported answers, which can vary over time despite the same level of joint degeneration. On the other hand, relying exclusively on X-ray findings in OA patients may not be sufficient, because patients with advanced osteoarthritis on X-ray may have mild or moderate pain and disability, while those with mild osteoarthritis on X-ray might be suffering from severe pain and disability. Therefore, clinical scales alone cannot be used to assessment of knee osteoarthritis. In the present study, we have proposed a new scale called "Khatib-Khaled Idlib University Scale" (KHIUS) which does not solely rely on the patient questionnaire but additionally utilizes clinical information based on radiographic finding, ESR values and physical examination. The goal of this study was to identify the risk factors associated with knee osteoarthritis (OA) in Northwest Syria and to assess KHIUS that we have proposed and determine its reliability in evaluating the severity of knee OA.

2. MATERIALS AND METHODS

The present study included 101 patients diagnosed with knee osteoarthritis based on simple X-Ray at the Orthopedic Clinic in Idlib University Hospital. The severity of osteoarthritic X-Ray grading was determined using the Kellgren and Lawrence (KL) classification, while the first-hour ESR value was also obtained.

Firstly, we collected personal information and risk factors of knee OA, including age, gender, Body Mass Index (BMI), and physical activity. Then, each patient, who suffered knee OA, was assessed using both WOMAC questionnaire and KHIUS criteria to determine knee OA severity.

WOMAC consists of 24 items divided into three subscales: pain, stiffness and disability. Each subscale consists of several items and points are

given for each item based on the patient's answer. The points are graded as follows: none (0), mild (1), moderate (2), severe (3) and extremely (4). The minimum total value in WOMAC is 0 while the maximum is 96.

KHIUS (Khatib-Khaled Idlib University Scale) includes 16 items divided into the following four subscales:

(A) Pain and disability: This subscale consist of eight items (Table 1), such as pain severity, pain and disability when standing, walking, getting up from a sitting position, at night, when ascending and descending stairs, in the bathroom, during housework, and during work and activity outside the house. Points are given for each item based on the patient's answer, and the points are graded as follows: none (1), mild (2), moderate (3), and severe (4). The minimum value in this group is 8, and the maximum is 32.

(B) Physical Examination: Physical examination is a crucial part of the knee OA assessment and includes six items, as shown in Table 2, including knee range of motion, swelling, patellar pressure test, joint line tenderness, flexion contracture, and knee stability. The minimum score in this group is 6 and the maximum is 24. Knee instability is an important factor in accelerating joint degeneration. Therefore, KHIUS awards 4 points when any form of knee instability is present.

(C) X-Ray grading: X-Ray grading, based on the KL classification, is divided into four grades, and because of its significance in the final assessment of knee OA, KHIUS assigns 2 points for KL grade I, 4 points for KL grade II, 8 points for KL grade III, and 12 points for KL grade IV, as shown in Table 3.

(D) Elevated ESR: Abnormally high inflammatory markers such as ESR have been shown to be associated with knee OA. Thus, KHIUS assigns 4 points when ESR is below 30 and 8 points when ESR is above 30 (after excluding other inflammatory diseases, malignant tumors, and rheumatoid arthritis), as shown in Table 3. The minimum value of KHIUS is 20 and the maximum value is 76. The knee OA severity grades based on KHIUS are presented in Table 4.

2.1. Statistical analysis

The statistical analysis was performed using the SPSS-25 software. Descriptive statistics were used. Nonparametric Mann-Whitney U-test and

Table 1. Variables of pain and disability group in KHIUS.

Pain and disability	none	mild	moderate	severe
Pain severity	1	2	3	4
standing	1	2	3	4
walking	1	2	3	4
Getting up from sitting position	1	2	3	4
At night	1	2	3	4
Housework	1	2	3	4
Outside house activities	1	2	3	4
Ascending and descending stairs	1	2	3	4

Table 2. Parameters of physical examination group in KHIUS.

Physical examination	none	mild	moderate	severe
Swelling	1	2	3	4
Joint line tenderness	1	2	3	4
Patellar pressure test	1	2	3	4
Flexion contracture	1	2	3	4
Range of motion	140-160	120-140	100-120	< 100
	1	2	3	4
Knee stability	normal		instability	
	1		4	

Table 3. Variables of X-Ray findings and grading as well as ESR analysis in KHIUS.

X-Ray grading			
Grade I	Grade II	Grade III	Grade IV
2	4	8	12
ESR analysis			
Less than 30		Equal or More than 30	
4		8	

Table 4. Knee OA severity grades according to KHIUS.

Knee OA grades	**KHIUS points**
Grade I: mild knee OA	20-33 points
Grade II: mild to moderate knee OA	34-47 points
Grade III: moderate to severe knee OA	48-61 points
Grade IV: severe knee OA	62-76 points

parametric Student's t-test were used to compare the variables. Correlations between WOMAC and KHIUS were tested by Pearson correlation. Spearman rank analysis was used to investigate correlations between WOMAC and KL-knee OA grading, and between KHIUS and KL-knee OA grading to determine the most closely scale to radiographic grades of knee osteoarthritis.

3. RESULTS

Table 5 shows that females in the sample had a significantly higher mean BMI value compared to males ($P < 0.01$), as the BMI values were divided into ranges and analyzed for their relationship with gender. In addition, the majority of cases (78%) were females. Females exhibit a higher susceptibility to developing OA [20]. This increased vulnerability in women may stem from various factors, such as thinner cartilage, a predisposition to varus malalignment, joint instability, and uneven mechanical loading [21]. Other factors include the loss of estrogen after menopause and the prevalence of obesity among women in northwest Syria. The mean age of the samples was 52.84 ± 9.74 years, with the age range of the participants from 25 to 80 years (Table 5).

The statistical data indicated that grade II left knee OA was the most prevalent among the participants as per KL classification. Furthermore, it was observed that most patients had mild daily

Table 5. Statistical analysis of age and BMI (body-mass index) groups.

	Males (*n* = 22)	**Females (*n* = 79)**	**P-Value**
BMI (Mean SD)	28.91 ± 4.87	35.11 ± 6.11	0.0001
	BMI		
BMI (kg\m²)	**Males**	**Females**	**Frequency/ percent**
20-24.99	6	3	9 (8.9%)
25-29.99	7	16	23(22.8%)
30-34.99	6	20	26 (25.7%)
35-39.99	3	25	28 (27.7%)
40 and more	0	15	15 (14.9%)
	Age		
Age (years)	**Frequency**		**Percent**
Equal and less 30	1		1%
31 – 40	10		9.9%
41 – 50	32		31.7%
51 – 60	35		34.7%
>60	23		22.8%

activity levels (see Table 6). The mean value of WOMAC in sample was 42.43 ± 8.18, total WOMAC values correlated with age (r = 0.35; p < 0.001) and BMI (r = 0.266; p = 0.007). Women and men had significantly different disease severity scores: 43.49 ± 7.77 and 38.59 ± 8.66, respectively (p = 0.023). The mean value of KHIUS was 52.27 ± 7, total KHIUS values correlated with age (r = 0.50; p <0.001) and BMI (r = 0.28; p = 0.004). Women and men had no significantly different disease severity scores: 52.92 ± 6.36 and 49.95 ± 8.7, respectively (p = 0.078). There was strong correlation (r = 80.3%, P < 0.001) between WOMAC and KHIUS (Table 7), thus suggesting that the KHIUS has construct validity for assessing the severity of knee OA (Figure 1). Additionally, the correlation coefficient between X-ray knee OA grading based on the KL classification and WOMAC in our sample was moderate (R: 50.9%, P < 0.001), while the correlation coefficient between X-ray KL knee OA grading and KHIUS was stronger (R: 75.7%, P < 0.001) (Table 7 and Figure 2).

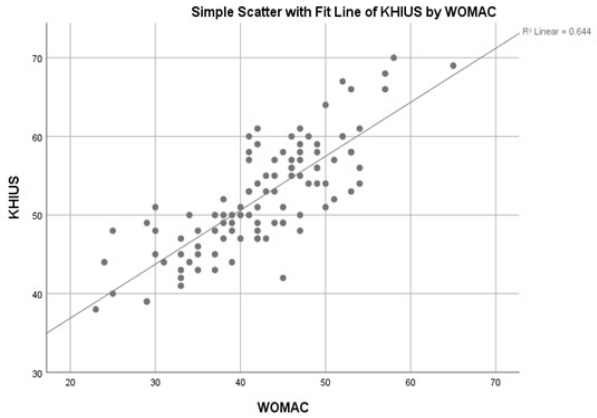

Fig. 1. Scatter plot of correlation of WOMAC to KHIUS.

4. DISCUSSION

The WOMAC score is a widely used clinical scale for evaluating the severity of knee and hip osteoarthritis on a global scale. Its reliability and validity have been established through numerous studies conducted worldwide, and it has been translated into multiple languages. According to previous research, the Cronbach's alphas for the WOMAC and Lequesne subscales ranged from 0.78-0.95 and 0.51-0.85 for hip OA, and 0.78-0.94 and 0.61-0.71 for knee OA, respectively [22]. Additionally, another study found that the test-retest reliability of all three WOMAC subscales (pain, stiffness, and physical function) was satisfactory, with ICCs of 0.86, 0.68, and 0.89, respectively [23]. The WOMAC score is extensively utilized for the pre- and post-evaluation of various therapeutic and surgical procedures [24, 25]. It involves asking patients a series of questions to assess the severity of pain, stiffness, and functional disability [26]. The WOMAC score is a subjective scale [27], and its effectiveness depends on the patient's cultural understanding of the questions asked. Cultural differences across the globe result

Table 6. Additional statistics.

		Frequency	Percentage
Daily activities	mild	72	71.3%
	moderate	26	25.7%
	high	3	3%
	total	101	100%
X-Ray grading according to Kellgren and Lawrence classification	Grade I	2	2%
	Grade II	49	48.5%
	Grade III	32	31.7%
	Grade IV	18	17.8%
	total	101	100%
Knee side affected	Right	29	28.7%
	Left	48	47.5%
	Both	24	23.8%
	total	101	100%

Table 7. Relationship between X-Ray grades with WOMAC and KHIUS.

		WOMAC (n = 101)	KHIUS (n = 101)
X-Ray grades (n=101)	r	0.509	0.757
	p	0.0001	0.0001
KHIUS	r	0.803	
	p	0.0001	

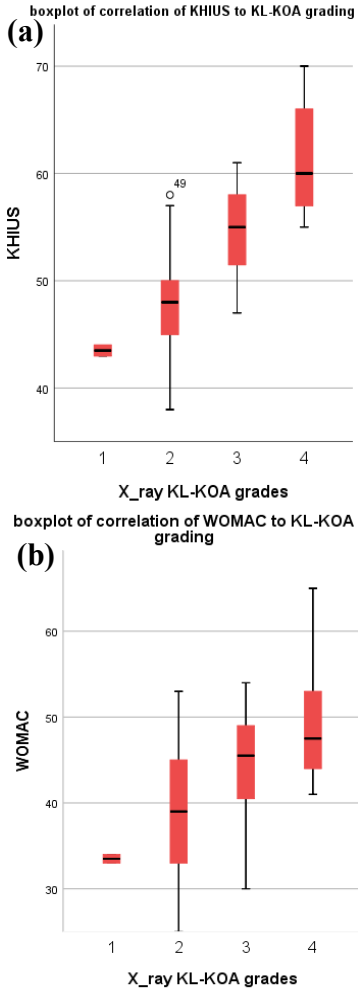

Fig. 2. Boxplots of correlation of (a) KHIUS and (b) WOMAC to KL knee osteoarthritis grades.

in varying responses to the questions asked which could potentially affect the accuracy of the score. In conflict areas, many patients may struggle to provide accurate responses due to their living conditions. For instance, people living in areas of protracted conflict do not have the luxury to sleep on beds. Rather, they sleep on the floor, thus making it impossible for them to answer questions related to getting up from a bed. Additionally, many people worldwide do not have access to cars, and therefore, those patients may not be able to accurately describe any difficulties they may face in using the car.

The WOMAC physical function subscale possesses a potential drawback due to its lack of clear distinction between the concepts of pain and function [28]. The WOMAC score is used to express the level of pain and disability experienced by patients with knee OA; however, this score may not always correlate with the radiological degree of the disease [29]. For instance, a low WOMAC score in some patients indicates mild degenerative disease, while radiographic grades in those patients indicates severe knee OA, hence, terms such as symptomatic knee osteoarthritis, radiographic knee osteoarthritis, and symptomatic radiographic knee osteoarthritis are widely used around the world [4]. To improve the accuracy of knee assessment, clinical data from physical examination such as range of motion, muscular atrophy, joint line tenderness, patellar tests, and knee stability should be included in the assessment. Moreover, the assessment should also include radiographic grades and the measurement of inflammatory markers, such as ESR, which have been shown to be important in the occurrence and progression of knee OA. Although rheumatoid arthritis (RA) is recognized as a severe inflammatory condition with elevated levels of ESR and CRP [30], OA has traditionally been viewed differently. It was believed that OA lacked significant inflammation, and therefore, serum markers of inflammation were not typically elevated in OA patients. However, recent studies have challenged this notion, revealing elevated levels of inflammatory markers, such as ESR and CRP, in individuals with OA. Studies have found a positive correlation between ESR levels and the severity of pain, stiffness, and functional disability [31, 32].

In this paper, we are proposing the KHIUS score to evaluate the severity of knee OA, which includes both subjective and objective measures. The subjective component assesses the patient's general daily activities without overly complex or repetitive questions, while the objective component includes physical examination data, radiographic

findings (based on the KL classification), and laboratory data (first-hour ESR value). The KHIUS score has a maximum value of 76, with 32 points allocated to the subjective component and 44 points to the objective component.

Of course, patients alone cannot determine their total KHIUS score since they can only use the subjective component to answer questions about their daily activities while they cannot determine the objective (clinical) component of data without the help of a clinician. However, orthopedic surgeons can use the entire KHIUS score to determine the severity of knee OA in their patients. By incorporating both subjective and objective measures, including patients' daily activities, physical examination data, radiographic findings, and laboratory data (such as ESR value), the KHIUS score offers orthopedic surgeons with valuable insights into the extent of knee OA and its impact on patients' functional status. This comprehensive evaluation enables clinicians to tailor treatment strategies to individual patients' needs, guiding decisions regarding the type and intensity of interventions required to manage knee OA effectively. Higher KHIUS scores may indicate more advanced disease and a greater need for aggressive interventions, such as surgical procedures. Conversely, lower KHIUS scores may suggest less severe disease and may prompt conservative management strategies, such as physical therapy or lifestyle modifications.

KHIUS score has its limitations. It may not be suitable for test-retest evaluation after treatment of knee OA due to the potential changes in objective data which comprises of radiographic findings, ESR value and physical examination findings. Therefore, the WOMAC score remains the most widely used method for test-retest evaluation after treatment in knee OA patients, while the KHIUS score may be considered the best method for determining the severity of knee OA.

Potential sources of bias or confounding factors that may affect the accuracy of the KHIUS score include its subjective nature, influenced by patients' interpretations and cultural differences, particularly in conflict areas or regions with diverse living conditions. Additionally, the reliance on clinicians for objective data introduces variability in scoring, limiting patient autonomy and potentially leading to subjective assessments. Measurement limitations, such as variations in imaging quality and inflammatory marker levels, can further impact score accuracy. Addressing these factors is crucial to enhance the reliability of the KHIUS score in assessing knee osteoarthritis severity and guiding treatment decisions effectively.

5. CONCLUSIONS

The Khatib-Khaled Idlib University Scale (KHIUS) was found to be closer to radiographic grades, indicating that it can be relied upon to assess knee OA severity and guide the method of treatment. Patients with knee OA can use clinical scales (such as WOMAC) to assess themselves, while orthopedic surgeons can use KHIUS after a complete examination and adding X-ray and laboratory test data. Therefore, KHIUS may serve as a reliable tool to assess knee OA severity in order to guide the method of treatment for patients with knee osteoarthritis. While our study utilized cross-sectional design to assess knee osteoarthritis severity using the WOMAC score, future research needs longitudinal or intervention studies for stronger causality evidence, providing insights into disease progression and interventions' impact for better prevention and treatment strategies.

6. ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from the patients. The study was approved by the Idlib University Research Ethics Committee. Patient privacy and data confidentiality were maintained in accordance with the Declaration of Helsinki.

7. ACKNOWLEDGEMENTS

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8. CONFLICT OF INTEREST

The authors declare no conflict of interest.

9. DECLARATION

We hereby declare that: (i) the results are original; (ii) the same material is neither published nor under

consideration elsewhere; (iii) approval of all authors have been obtained; and (iv) in case the article is accepted for publication, its copyright will be assigned to Pakistan Academy of Sciences.

10. REFERENCES

1. M. Sowers. Epidemiology of risk factors for osteoarthritis: systemic factors. *Current Opinion in Rheumatology* 13: 447–451 (2001).
2. M. Fransen, L. Bridgett, L. March, D. Hoy, E. Penserga, and P. Brooks. The epidemiology of osteoarthritis in Asia. *International Journal of Rheumatic Diseases* 14(2): 113–121 (2011).
3. T. Neogi, and Y. Zhang. Epidemiology of Osteoarthritis. *Rheumatic Disease Clinics of North America* 39(1): 1–19 (2013).
4. S. Lee, and S.-J. Kim. Prevalence of knee osteoarthritis, risk factors, and quality of life: The Fifth Korean National Health And Nutrition Examination Survey. *International Journal of Rheumatic Diseases* 20(7): 809–817 (2017).
5. S. Muraki, H. Oka, T. Akune, A. Mabuchi, Y. En-yo, M. Yoshida, A. Saika, T. Suzuki, H. Yoshida, H. Ishibashi, S. Yamamoto, K. Nakamura, H. Kawaguchi, and N. Yoshimura. Prevalence of radiographic knee osteoarthritis and its association with knee pain in the elderly of Japanese population-based cohorts: The ROAD study. *Osteoarthritis and Cartilage* 17(9): 1137–1143 (2009).
6. J. Bedson, and P.R. Croft. The discordance between clinical and radiographic knee osteoarthritis: A systematic search and summary of the literature. *BMC Musculoskeletal Disorders* 9: 116 (2008).
7. N. Verzijl, R.A. Bank, J.M. TeKoppele, and J. DeGroot. AGEing and osteoarthritis: A different perspective. *Current Opinion in Rheumatology* 15(5): 616–622 (2003).
8. A.S. Anderson, and R.F. Loeser. Why is osteoarthritis an age-related disease? *Best Practice & Research Clinical Rheumatology* 24(1): 15–26 (2010).
9. J.A. Gokhale, S.R. Frenkel, and P.E. Dicesare. Estrogen and osteoarthritis. *American Journal of Orthopedics (Belle Mead, N.J.)* 33(2): 71–80 (2004).
10. J. Sellam, and F. Berenbaum. Is osteoarthritis a metabolic disease? *Joint Bone Spine* 80(6): 568–573 (2013).
11. N. Zapata-Linares, F. Eymard, F. Berenbaum, and X. Houard. Role of adipose tissues in osteoarthritis. *Current Opinion in Rheumatology* 33(1): 84–93 (2021).
12. T.D. Spector, P.A. Harris, D.J. Hart, F.M. Cicuttini, D. Nandra, J. Etherington, R.L. Wolman, and D.V. Doyle. Risk of osteoarthritis associated with long-term weight-bearing sports: A radiologic survey of the hips and knees in female ex-athletes and population controls. *Arthritis & Rheumatism* 39(9): 988–995 (1996).
13. E. Shorter, A.J. Sannicandro, B. Poulet, and K. Goljanek-Whysall. Skeletal Muscle Wasting and Its Relationship With Osteoarthritis: a Mini-Review of Mechanisms and Current Interventions. *Current Rheumatology Reports* 21(8): 40 (2019).
14. B. Yucesoy, L.E. Charles, B. Baker, and C.M. Burchfiel. Occupational and genetic risk factors for osteoarthritis: A review. *Work* 50(2): 261–273 (2015).
15. E.M. Roos, and L.S. Lohmander. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint Injury to Osteoarthritis. *Health and Quality of Life Outcomes* 1: 64 (2003).
16. E.M. Roos, H.P. Roos, L.S. Lohmander, C. Ekdahl, and B.D. Beynnon. Knee Injury and Osteoarthritis Outcome Score (KOOS)—Development of a Self-Administered Outcome Measure. *Journal of Orthopaedic & Sports Physical Therapy* 28(2): 88–96 (1998).
17. D.W. Murray, R. Fitzpatrick, K. Rogers, H. Pandit, D.J. Beard, A.J. Carr, and J. Dawson. The use of the Oxford hip and knee scores. *The Journal of Bone and Joint Surgery - British Volume* 89(8): 1010–1014 (2007).
18. N.J. Collins, D. Misra, D.T. Felson, K.M. Crossley, and E.M. Roos. Measures of knee function: International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, Knee Injury and Osteoarthritis Outcome Score (KOOS), Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS-PS), Knee Ou. *Arthritis Care & Research* 63(S11): S208–S228 (2011).
19. B. Eftekhar-Sadat, S.H. Niknejad-Hosseyni, A. Babaei-Ghazani, V. Toopchizadeh, and H. Sadeghi. Reliability and validity of Persian version of Western Ontario and McMaster Universities Osteoarthritis index in knee osteoarthritis. *Journal of Analytical Research in Clinical Medicine* 3(3): 170–177 (2015).
20. E.R. Vina, and C.K. Kwoh. Epidemiology of osteoarthritis: literature update. *Current Opinion in Rheumatology* 30(2): 160–167 (2018).
21. M. Tschon, D. Contartese, S. Pagani, V. Borsari, and M. Fini. Gender and Sex Are Key Determinants in Osteoarthritis Not Only Confounding Variables.

A Systematic Review of Clinical Data. *Journal of Clinical Medicine* 10(14): 3178 (2021).

22. S. Basaran, R. Guzel, G. Seydaoglu, and F. Guler-Uysal. Validity, reliability, and comparison of the WOMAC osteoarthritis index and Lequesne algofunctional index in Turkish patients with hip or knee osteoarthritis. *Clinical Rheumatology* 29(7): 749–756 (2010).
23. F. Salaffi, G. Leardini, B. Canesi, A. Mannoni, A. Fioravanti, R. Caporali, G. Lapadula, and L. Punzi. Reliability and validity of the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index in Italian patients with osteoarthritis of the knee. *Osteoarthritis and Cartilage* 11(8): 551–560 (2003).
24. L.C. Walker, N.D. Clement, M. Bardgett, D. Weir, J. Holland, C. Gerrand, and D.J. Deehan. The WOMAC score can be reliably used to classify patient satisfaction after total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 26(11): 3333–3341 (2018).
25. E. Roos, M. Klässbo, and L.S. Lohmander. WOMAC Osteoarthritis Index: Reliability, validity, and responsiveness in patients with arthroscopically assessed osteoarthritis. *Scandinavian Journal of Rheumatology* 28(4): 210–215 (1999).
26. N.F. Woolacott, M.S. Corbett, and S.J.C. Rice. The use and reporting of WOMAC in the assessment of the benefit of physical therapies for the pain of osteoarthritis of the knee: findings from a systematic review of clinical trials. *Rheumatology* 51(8): 1440–1446 (2012).
27. L.C. Walker, N.D. Clement, M. Bardgett, D. Weir, J. Holland, C. Gerrand, and D.J. Deehan. Correction to: The WOMAC score can be reliably used to classify patient satisfaction after total knee arthroplasty. *Knee Surgery, Sports Traumatology, Arthroscopy* 27: 340–340 (2019).
28. D.K. White, and H. Master. Patient-Reported Measures of Physical Function in Knee Osteoarthritis. *Rheumatic Disease Clinics of North America* 42(2): 239–252 (2016).
29. W. Steenkamp, P.A. Rachuene, R. Dey, N.L. Mzayiya, and B.E. Ramasuvha. The correlation between clinical and radiological severity of osteoarthritis of the knee. *SICOT-J* 8: 14 (2022).
30. K. Shimada, A. Komiya, N. Yokogawa, J. Nishino, S. Sugii, and S. Tohma. Impact of the size and number of swollen joints on serum C-reactive protein level and erythrocyte sedimentation rate in rheumatoid arthritis: a cross-sectional study in Japan. *Clinical Rheumatology* 36(2): 427–431 (2017).
31. M. Hanada, M. Takahashi, H. Furuhashi, H. Koyama, and Y. Matsuyama. Elevated erythrocyte sedimentation rate and high-sensitivity C-reactive protein in osteoarthritis of the knee: relationship with clinical findings and radiographic severity. *Annals of Clinical Biochemistry: International Journal of Laboratory Medicine* 53(Pt 5): 548–553 (2016).
32. D.C. Sanchez-Ramirez, M. van der Leeden, M. van der Esch, M. Gerritsen, L.D. Roorda, S. Verschueren, J. van Dieen, J. Dekker, and W.F. Lems. Association of serum C-reactive protein and erythrocyte sedimentation rate with muscle strength in patients with knee osteoarthritis. *Rheumatology* 52(4): 727–732 (2013).