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Correlation between radiologic and clinical features with quality of life in knee osteoarthritis: A Literature Review

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Abstract

Osteotarthritis (OA) is one of the most common inflammatory joint diseases and rheumatic musculoskeletal conditions worldwide. OA is the 11th most disabling disease in the world. Knee OA is the most common joint condition, accounting for 83% of cases out of 4% of the global population. Diagnosing OA typically begins with history taking of patient, physical examinations, and supportive examination guided by the Indonesian Rheumatology Association. WOMAC index is a widely used patient-reported tool to assess pain, stiffness, and physical function in knee OA patients. Additionallly, knee OA is often evaluated using anteroposterior radiographs to identify osteophytes and joint space narrowing. The Kellgren-Lawrence scoring system is commonly employed to classify radiographis severity. Knee OA is a chronic condition that impairs daily activities and significantly diminishes quality of life (QoL). The SF-36 questionnaire is frequently used to evaluate QoL, providing a holistic view of health status and guiding patient management. Based on the high prevalence of knee OA, the variety of instruments used in determining the severity of OA both clinically and radiologically, the variety of risk factors for OA events, and the lack of research related to the relationship between clinical and radiological images with the quality of life of patients, researchers will analyse the correlation between radiological images (Kellgren-Lawrence) and clinical images (WOMAC) with QoL (SF-36). However, more extensive and in-depth study is still required to determine which risk factors have a significant impact on the correlation of this three components in knee OA patients.

Keywords: Knee OA; WOMAC; Kellgren-Lawrence; SF-36

1. Introduction

Osteoarthritis (OA) is one of the most prevalent arthritis and rheumatic musculoskeletal disorders in the world [1]. OA ranks as the 11th most debilitating disease in the world [2]. Globally, OA affected 527.81 million people in 2019 with prevalence in men and women over 60 years of age at 9.6% and 18% [3, 4]. Meanwhile, OA has become one of the ten most debilitating diseases in developed countries [4]. In Indonesia, the prevalence of OA in men is 15.5% and women 12.7% [5]. This figure will continue to increase with age by 18.6% at the age of more than 65 years and 18.9% at the age of more than 75 years [6]. OA commonly affects the knee, hip, fingers and neck joints [7]. Knee OA is the most common joint disorder with a prevalence of 83% of cases out of 4% of the world's population experiencing OA [8].

The diagnosis of OA begins with a history, physical examination, and supporting examination according to the recommendations of the Indonesian Rheumatology Association [9]. One of the commonly used patient-based subjective clinical instruments to aid the diagnosis of knee OA is the Western Ontario and McMaster Universities (WOMAC). This instrument is the most frequently used tool to assess dysfunction status and symptoms in patients with knee OA. The

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main supporting examination often used in diagnosing knee OA is the anteroposterior radiographic modality [10]. This radiologic examination aims to evaluate osteophytes and joint space narrowing, with the Kellgren-Lawrence scoring system as a tool to classify the severity of knee OA radiographs [11].

Knee OA is a chronic joint disease that has an impact on reducing the function of the patient's daily activities and contributes negatively to reducing the patient's Quality of Life (QoL) or quality of life [12]. Assessment of patient QoL can use the Short Form-36 (SF-36) questionnaire which is a generic instrument for assessing the health status and quality of life of individuals. The use of the SF-36 instrument can help the management of knee OA patients in improving patient QoL.

Based on the high prevalence of knee OA, the diversity of tools used in determining the severity of OA both clinically and radiologically, the diverse risk factors for OA events, and the lack of literature review related to the relationship between clinical and radiological images with the quality of life of patients are the reasons for researchers to analyze the correlation between radiological images (Kellgren-Lawrence Scoring System) and clinical images (WOMAC Score) with quality of life (SF- 36) in knee OA patients.

2. Review Content

2.1. Knee Osteoarthritis

2.1.1. Definition

Arthritis is the occurrence of inflammation (inflammation) and swelling in the joints. One of the most common types of arthritis, which is chronic, has a significant impact on health is osteoarthritis (OA) [9]. Osteoarthritis (OA) is a degenerative joint disease characterized by progressive destruction of joint cartilage and accompanied by changes in the underlying bone structure [2, 13]. Knee osteoarthritis (OA) is one of the most common types of OA and involves joint damage in the knee area. Knee OA often affects the medial tibiofemoral (varus), lateral tibiofemoral (valgus), femoropatellar, and bony enlargement compartments [9].

2.1.2. Pathophysiology

OA is a disease that affects all components of the joint, including in and around it [2]. Damage from OA involves degradation of joint cartilage, thickening of subchondral bone, osteophyte formation, ligament damage, synovial tissue inflammation, hypertrophy in the joint capsule, to changes in periarticular muscles, bursa, nerves, and fat pads [14]. In the knee joint, adipose tissue known as the infrapatellar fat pad contains inflammatory cells that trigger pain at the front of the knee. This inflammatory process contributes to the development of knee OA [15].

2.1.3. Risk Factor of Knee Osteoarthritis

Modifiable Risk Factor

Muscle Weakness
The extensor muscles in the knee function in absorbing shock and stabilizing the knee during loading so that if there is muscle weakness, changes in muscle activation patterns, and proprioceptive deficits can cause excessive mechanical stress on the articular cartilage resulting in knee OA [16].

Weight
Obese individuals with BMI > 30 kg/m2 , have been shown to have limitations in tissue perfusion and reduced overall cartilage health resulting in an increased risk of knee OA. In contrast, individuals who successfully lost weight had greater improvements in knee pain, function, mobility and compressive strength [17].

Metabolic Syndrome
Metabolic syndromes such as obesity, hypertension, dyslipidemia, and impaired glucose tolerance not only increase the risk of OA, but also its progression [16].

Articular Trauma
Articular trauma significantly accelerates progression to OA at various joint locations. Individuals who experience knee trauma are 4.2 times more at risk of developing knee OA. The type of trauma suffered also affects the progression of OA. Injuries to ligaments, tendons, meniscus and fractures increase the risk of knee OA [17].

Occupation
Occupations that involve the use of heavy physical qualities affect the incidence of OA. Repetitive movements, kneeling, vibrating, squatting, standing, frequent bending of the knees while lifting weights for a long time are physical work associated with cartilage degeneration thus increasing the incidence of OA [16].

Non-Modifiable Risk Factor

Age
The prevalence of OA is rare at ages under 40 years, but often occurs at ages over 60 years. Increasing age affects the thinning of cartilage and weakening of muscles, thus disrupting the stability of major joints such as the knee joint [18].

Gender
The prevalence of knee OA in women is higher than in men. Women lose knee articular cartilage at a faster rate than men. This is because the availability of estrogen and growth hormones in women tends to decrease with age. Female articular chondrocytes are also less responsive to vitamin D metabolites thus increasing cartilage degeneration resulting in knee OA [16].

Race
Based on a study by the National Health and Nutrition Examination Survey I (NHANES I), African-American women are more likely to have knee OA compared to white men [19]. Some Asian populations are at lower risk of developing OA [1].

Genetic
Individuals who have family members with a history of OA tend to be at risk of developing OA [1]. In the Caucasian population, the locus that is significantly susceptible to the incidence of knee OA is chromosome 7q22. Genetic polymorphisms are also a genetic predisposing factor in knee OA [16].

2.1.4. Classification of Knee Osteoarthritis

Based on etiology, OA can be classified into primary OA and secondary OA. Primary knee OA is the degeneration of articular cartilage without an obvious cause, often associated with ageing and wear and tear of the bone. Meanwhile, secondary knee OA results from degeneration of articular cartilage with an identifiable cause, such as abnormal force concentration post-trauma, post- surgery, varus/valgus malposition, and others [13].

2.1.5. Sign and Symptom of Knee Osteoarthritis

The triad of OA symptoms includes joint pain, stiffness, and limitation of motion. Patients may also experience bone swelling, joint deformity and instability. Typical signs and symptoms, such as bone enlargement, crepitus, effusion (non-inflammatory), limited range of motion, tenderness at the joint line, and pain on passive movements are also often found [2]. The main sign and symptom of knee OA is knee pain. The pain occurs gradually and worsens during strenuous and prolonged activities such as bending or climbing stairs. In addition, there is also stiffness and swelling of the knee [13].

2.1.6. Diagnose of Knee Osteoarthritis

The diagnosis of knee OA is established through the stages of history taking, physical examination, elimination of differential diagnosis, supporting examination, as well as special attention to clinical symptoms and risk factors that affect OA management. The classification of knee OA based on the American College of Rheumatology (ACR) criteria is used as a uniformity and reference for the diagnosis of knee OA. The following is a classification table of knee OA diagnosis based on ACR [20].

Table 1 Classification of Knee OA Diagnose Based on ACR ICD-10 Code: M17

Based on Clinical Criteria	**Based on Clinical and Radiological Criteria**	**Based on Clinical and Laboratorial Criteria**
Knee joint pain with at least 3 of the 6 criteria below: 1. Age > 50 years 2. Bone edge tenderness	Knee joint pain with osteophytes plus meet the criteria of at least 1 of the 3 below: 1. Age > 50 years 2. Joint stiffness < 30 minutes	Knee joint pain with at least 5 of the 9 criteria below: 1. Age > 50 years 2. Bone edge tenderness

3. Joint stiffness < 30 minutes 4. Bone enlargement of the knee joint 5. Crepitus during active movement6. The synovium of the knee joint is not palpably warm 6. The synovium of the knee joint is not palpably warm Description: 95% Sensitivity 69% Specificity	3. Crepitus during active movement Description: 91% Sensitivity 86% Specificity	3. Joint stiffness < 30 minutes 4. Bone enlargement of the knee joint 5. Crepitus during active movement6. The synovium of the knee joint is not palpably warm 6. The synovium of the knee joint is not palpably warm 7. ESR <40 mm/hour 8. Rheumatoid Factor (RF) <1:40 9. OA synovium analysis Description: 92% Sensitivity 75% Specificity

2.1.7. Management of Knee Osteoarthritis

Currently, there is no treatment that can overcome the effects of OA. Symptomatic management aims to manage symptoms and slow disease progression. The basic principles of OA management, namely patients can understand the basic course of the disease, provide psychological support to patients, control pain, suppress inflammation, support patients to be physically active to maintain joint function and prevent deformities, correct deformities, improve function, strengthen muscle weakness, avoid excessive therapy with pharmacological drugs, rehabilitate patients. OA management is divided into two, namely non-operative and operative management. The following are the types of OA management [21].

Table 2 Knee OA Management

Non-Operative Management	**Operative Management**
Non-Pharmacological Lifestyle modification: education, activity modification, weight loss, use of walking aids. The use of shoes and orthoses Use of a brace Rehabilitation	Arthroscopy, debridement, lavage Osteotomy Arthroplasty Resection arthroplasty Symptomatic chondral focal defect Meniscal allograft transplantation
Pharmacological NSAID/NSAID Analgesics Topical analgesics Intra-articular therapy Hyaluronate Corticosteroids	

2.2. WOMAC Index

The WOMAC Index (Western Ontario and McMaster Universities Ostheoarthritis Index) is a clinical evaluation tool in the form of a questionnaire used to assess the severity of OA patients [6]. Since its introduction in 1998, this index has become one of the most widely used and recommended instruments because it has high sensitivity and specificity in assessing patient conditions [22]. The WOMAC instrument focuses on evaluating knee and hip OA patients mainly on the incidence of pain, stiffness, and activity limitation [23]. In addition, the use of the WOMAC index can also be used to evaluate knee OA before and during follow-up treatment both non-operative and operative [22].

The WOMAC index consists of 24 items divided into 3 subscales, namely pain, stiffness, and physical function. The pain subscale contains 5 items related to walking, using stairs, sitting or lying in bed, and standing upright. The stiffness subscale contains 2 items in the form of after waking up at the beginning of the day and during the day. The physical

function subscale contains 17 items, namely using stairs, getting up from sitting, standing, bending, walking, getting in/out of the car, shopping, putting on/removing socks, getting out of bed, lying in bed, entering/exiting the bathroom, sitting, entering/exiting the toilet, heavy household tasks, light household tasks [24].

Calculation of the WOMAC index uses a Likert scale in the form of a numerical score of 0 – 4 according to the severity level consisting of none, mild, moderate, severe, and extreme. The minimum score is 0 and the maximum is 96 with 20 points for pain, 8 points for stiffness, and 68 points for physical function [11].

2.3. Kellgren-Lawrence Grading System

Radiographic imaging is necessary in evaluating knee OA. Recommended positions for radiographic imaging of knee OA include anteroposterior (AP) standing position, lateral with extension, patella wide view, and posteroanterior (PA) position with a 45-degree angle at the knee. These positions provide a better assessment of the weight-bearing surface of the knee, the degree of deformity, as well as the overall alignment of the lower extremity. On radiographs of knee OA, some typical findings that can be identified include narrowing of the joint gap, osteophyte formation, subchondral sclerosis and subchondral cysts. For radiographic imaging results to accurately depict joint space narrowing, the patient must be in a standing position. Imaging performed in the supine position does not provide a picture that is consistent with the condition of the knee joint, so it cannot be used as a precise evaluation of knee OA [13].

Kellgren-Lawrence is a grading system used to determine the severity of knee OA since 1957. This grading system is widely used in clinical practice to evaluate radiographs and diagnose knee OA. The Kellgren-Lawrence classification not only helps in determining the stage of knee OA progression, but also guides clinical decision-making and the choice of non-operative and surgical therapies. The Kellgren-Lawrence grading system has the highest correlation coefficient in diagnosing knee OA compared to diagnosing other types of OA [10]. The following is an explanation and division of severity levels in the Kellgren- Lawrence grading system based on anteroposterior knee X-rays [25, 10].

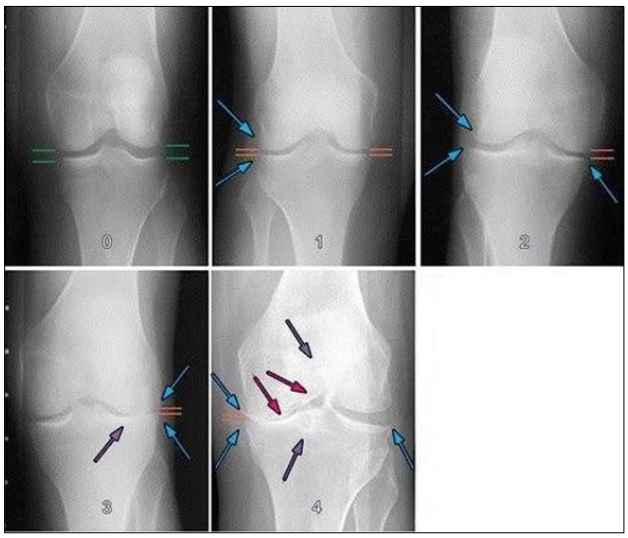

Figure 1 Knee X-Ray Based on Kellgren-Lawrence Scoring System

Table 3 Kellgren-Larence Scoring System

Stage	**0**	**1**	**2**	**3**	**4**
Classification	**Normal**	**Doubtful**	**Mild**	**Moderate**	**Severe**
Description	No features of OA	Narrowing of the joint gap and doubtful formation of osteophytes	Possible narrowing of the gap joint with obvious osteophyte formation	Narrowing of the joint gap is obvious, moderate osteophytes are formed, some sclerosis, and possible deformity at the end of the bone	Large osteophyte formation, narrowing of the joint gap, joint narrowing followed by signs of sclerosis, and deformity at the end of the bone is obvious

2.4. SF-36 Questionnaire

Quality of Life (QoL) is a concept of population and individual well-being against positive and negative elements at a certain point in time. Common aspects of QoL include physical, mental, spiritual personal health, educational status, social status, work environment, sense of security, safety, autonomy in making decisions, sense of belonging, and physical environment [26].

Knee OA is a chronic joint disease that causes functional impairment of work and causes pain so that patients experience limitations in daily activities. This has a negative impact on social, psychological aspects, and reduces the patient's quality of life [12]. According to the World Health Organization (WHO), health is a state of a person not only the absence of disease, but also a person feels well in physical, mental, and social aspects. Therefore, researchers developed instruments based on the concept of Health Related Quality of Life (HRQoL) to assess QoL which includes aspects of physical, mental and social well-being [27]. Instruments in evaluating QoL can be divided into two types, namely generic instruments to identify the impact of the disease on the patient's general health and specific instruments to measure the impact of the disease on QoL domains that are directly affected by the disease itself.

The Short Form-36 (SF-36) is the most commonly used generic instrument questionnaire and the gold standard for assessing QoL worldwide [28]. The SF-36 was introduced in the 1980s. This questionnaire is used to assess the health status and QoL of individuals. The SF-36 consists of 36 short questions divided into 8 dimensions, including physical function, social function, physical role, body pain, mental health, emotional role, vitality, and general health [22]. The SF-36 score uses an ordinal scale between 0-100, the higher the score the better the patient's QoL. It also applies vice versa [29].

2.5. Correlation Kellgren-Lawrence Grading System with WOMAC Index

Based on research conducted by Cubukcu et al [30], no correlation was found between the severity of WOMAC index and radiological grade based on the Kellgren-Lawrence scoring system. Nonetheless, the Kellgren-Lawrence scoring system and WOMAC index severity are important for assessing knee OA disease progression. Seifeldein et al [11] also found that there was no relationship between WOMAC subclasses and the Kellgren-Lawrence scoring system. Similar results were obtained by Kocak, et al [31] who reported that there was no correlation between pain and functional disability with poor radiological images . This is likely due to the absence of pain fibers in the hyaline cartilage of the joint so the cartilage is not the main source of knee OA pain [32]. Radiologic features of knee OA patients do not show a strong relationship with signs and symptoms of knee OA. However, there is a correlation with signs and symptoms of knee OA at higher levels of Kellgren-Lawrence scores at stages 3 and 4 [31]. Therefore, the treatment of knee OA can be planned according to the clinical features and functional status, not only based on radiological findings [30].

A potential factor that causes the relationship between radiologic images and clinical images, especially pain, to be insignificant is the often insufficient number of radiographic photo-taking positions in the study, such as data from patients with very painful clinical images, so that the power to detect the relationship between radiologic images based on the Kellgren-Lawrence system and the overall clinical picture is limited. In addition, the varied and broad ways of defining pain led to inconsistencies that contributed to the insignificance of the relationship between radiologic images and the clinical picture of patients. Other factors such as age, ethnicity, and gender may influence the relationship between radiological images and clinical pain in patients with knee OA [33].

Further research shows that the severity of Kellgren Lawrence is related to biological changes such as proinflammatory cytokines and telomere size. Telomere size decreases with an increase in the severity of Kellgren Lawrence, this telomere shortening indicates premature aging, thus exacerbating chondrocyte aging and degenerative changes in the joint. Cytokines as signaling molecules of inflammation and immune response also contribute to increased pain in patients with higher levels of Kellgren-Lawrence [34].

The limitations of radiographic modalities also influenced the results of the study. Radiography has limitations in detecting soft tissue changes directly, such as the measurement of joint space narrowing has low sensitivity in detecting soft tissue changes and the presence of subchondral sclerosis, cysts, as well as osteophytes have low sensitivity to cartilage degeneration while these things are the focus in the Kellgren Lawrence scoring system so that it can affect the classification results of radiological images with insignificant clinical images. In addition, radiographs also have limitations in recognizing signs in the early stages of knee OA disease. This is because radiographic modalities are more effective in detecting secondary changes, such as osteophyte formation, cartilage loss, and meniscus extrusion that usually occur in advanced knee OA. The insignificance between radiologic features and knee OA severity may also be influenced by pathophysiologic differences in the various phenotypes [35].

2.6. Correlation Kellgren-Lawrence Grading System with SF-36

The relationship between the degree of radiologic classification in knee OA events and the quality of life of patients is still not widely known. Based on a cohort study in Southern Sweden, it was found that knee OA patients with radiologic abnormalities and knee pain had a lower quality of life compared to knee OA patients who only had radiologic abnormalities without knee pain. Another study using the same two parameters showed that the relationship between radiological images using the Kellgren-Lawrence scoring system with SF-36 was found to be significant, especially in the social function dimension [36].

Sananta et al [37] also reported a significant negative relationship between knee OA severity and patient quality of life in the domains of physical function and general health, while the relationship was not significant in the domains of physical limitations, body pain, vitality, social function, emotional limitations, and mental health. Another comparative study in knee OA patients found a significant negative relationship in the domains of physical function, physical limitations, general health, social function, and emotional limitations [38].

The severity of knee OA based on the Kellgren Lawrence grading system reflects the patient's limitations. The higher the severity of knee OA, the worse the pain and physical limitations. A higher Kellgren-Lawrence score also affects general health perception. This is evidenced by patient reports of increased pain and disability which adversely affect patient perception of general health status [37, 38]. Overall, the study showed a negative correlation between the severity of knee OA based on the Kellgren-Lawrence radiological picture and the decline in patient quality of life [39]. The significant negative correlation between the Kellgren-Larence scoring system and SF-36 can be caused by various factors, such as gender, age, obesity, hypertension, diabetes mellitus, and other diseases related to the patient's social life [40]. Knee OA greatly affects the patient's quality of life related to physical health [34]. Based on the above evidence, it can be concluded that the higher the degree of Kellgren Lawrence knee OA, the lower the total SF-36 score and the worse the patient's QoL.

2.7. Correlation WOMAC Index with SF-36

The use of the WOMAC instrument provides in-depth insight into the specific effects of knee OA, while the SF-36 provides a broader picture of general health and quality of life [41]. These two instruments complement each other in the diagnosis of knee OA, provision of healthcare, and comprehensive understanding of the patient's condition.

Pain in knee OA patients can interfere with the patient's daily activities, social interactions, and can cause economic burdens so that the patient's quality of life decreases. Research shows there is a significant relationship between the severity of knee OA based on the WOMAC score and the patient's quality of life [42]. The variables in the WOMAC score, namely pain, stiffness, and physical function, correlate significantly with the dimensions of physical function and pain areas in patients' quality of life as assessed by the SF-36. In addition, there is also a good to moderate correlation between WOMAC and the physical role dimension on the SF-36 [43, 44]. In a study related to the impact of neuropathic pain in knee OA, it was found that severity based on WOMAC scores was associated with poorer quality of life in patients with or without neuropathic pain [45]. Higher knee OA symptom severity scores were associated with worse pain, sleep quality, quality of life, and depression- anxiety scores [45].

However, a study showed an insignificant relationship between the total WOMAC score and several domains on the SF-36, such as the domains of physical function, physical limitations, body pain, general health, vitality, social function, emotional limitations, and mental health [46]. However, a negative correlation was found between the two variables, meaning that the higher the total WOMAC score, the lower the patient's quality of life and vice versa. Intense pain and pain in knee OA patients can cause decreased mobility and decreased knee joint strength so that physical function decreases resulting in physical limitations. The consequences of this result in reduced patient independence in carrying out daily activities and have an impact on decreased quality of life [47].

Knee pain, decreased mobility function, stiffness, and decreased quadriceps muscle strength are often associated with knee OA. These conditions can lead to physical disability, limiting mobility function which results in a decrease in the patient's quality of life and work capacity function [38]. Therefore, the more severe the clinical picture of a knee OA patient, the more the patient's quality of life decreases.

3. Conclusion

In conclusion, this paper discusses the correlation between radiological features based on the Kellgren-Lawrence scoring system and clinical features based on the WOMAC index with QoL based on the SF-36 questionnaire in knee OA patients. There was an insignificant relationship between the Kellgren Lawrence scoring system and the clinical picture

of the WOMAC index of knee OA patients. Meanwhile, there was a negative relationship between Kellgren Lawrence scoring system and SF-36 questionnaire and WOMAC index and SF-36 questionnaire. This paper highlights the importance of the relationship between radiological features, clinical features, and QoL of knee OA patients to help therapeutic and non-therapeutic interventions in knee OA cases. Therefore, further research is needed regarding the correlation of radiological features based on the Kellgren-Lawrence scoring system and clinical features based on the WOMAC index with QoL based on SF-36 questionnaire by collecting a larger and optimal sample size, as well as further statistical correlation analysis between the relationship of each domain in the SF-36 so that it represents better results in radiological images, clinical features, and QoL features.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest to be disclosed.

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