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Role of global femoral cartilage in assessing severity of primary knee osteoarthritis

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Abstract

Background/objective: Osteoarthritis is a degenerative joint disease marked by structural changes in the joint. Radiological evaluation can be used to assess structural changes. Pain, inflammation, and stiffness are common clinical symptoms, leading to limitations in daily activities. Ultrasound, unlike traditional radiography, allows for a direct examination of changes in soft tissues. In addition, it is sensitive in detecting osteophytes as well as identifying early OA changes in femoral cartilage associated with clinical manifestations and function.

Results: A cross-sectional study of 40 patients with primary KOA diagnosed according to the American College of Rheumatology (ACR) criteria. After radiographic evaluation using Kellgren-Lawrence (K-L) scale and US examination assessing global femoral hyaline cartilage (GFC), osteophytes, meniscal extrusion, effusion, and Baker's cyst of the most symptomatic knee, there was significant correlation between (K-L) grading and (GFC) ultrasonographic grading ($p < 0.001$). After assessment of pain and functional disability using Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale, there was significant correlation between KL and GFC grading with age ($p < 0.001$ for both), disease duration ($p < 0.001$ for both) as well as WOMAC total scores ($p < 0.001$ for both). GFC grading was the only independent predictor relative to other ultrasonographic variables for WOMAC total score ($p < 0.001$).

Conclusions: US is a valid tool to evaluate knee joint space and is well correlated with radiographic images. KOA severity assessed by KL grading and GFC ultrasonographic grading showed good correlation with age, duration of the disease, pain intensity, and functional disability.

Keywords: Knee, Osteoarthritis, Ultrasound

Background

Knee osteoarthritis (KOA) is one of the most frequent degenerative joint disease in the elderly, causing pain and limitation of joint function [1]. Previous research has shown that only about half of patients with knee pain suspecting KOA will have radiographic changes [2]; moreover, only about half of patients with radiographic KOA might experience pain [3]. There is moderate relationship between the radiographic degree of KOA and the level of

pain [4, 5]. Conventional radiography (CR) was the first imaging modality used to diagnose KOA, which assesses the bone structure and severity of the disease. The evaluation of both osteophytes and joint space narrowing is the mainstay of CR assessment of KOA [6], although has a limited ability to image soft tissues and gives indirect evidence of cartilage destruction [7, 8].

Ultrasonography (US) has recently improved KOA diagnosis and management [9]. It is a practical, reliable, noninvasive, cheap, readily available, valid tool for assessing KOA and does not need the use of ionizing radiation [10]. Current US technology has a number of advantages, including the capacity to identify osteophytes, articular cartilage degeneration, meniscal and ligament tears, bursitis, effusion, and interventional operations [11]. Several

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researches have reported significant correlations between KOA characteristics as detected by US and CR, especially for osteophytes where ultrasound is more sensitive than radiography [12].

The aim of this study was to evaluate the association between clinical examination and functional disability with ultrasonographic and radiographic findings in patients suffering from primary (KOA).

Methods

This cross-sectional study was performed at the Physical Medicine, Rheumatology and Rehabilitation outpatient clinics in the Main University Hospital. Forty patients fulfilling the ACR criteria for KOA [13] were enrolled in the present study. Patients with secondary KOA, history of previous knee surgery, and trauma were all ruled out.

Patient evaluation was performed following the International Classification of Functioning, Disability and Health (ICF) [14]; all patients were subjected to detailed local knee assessment, and WOMAC scores were used to assess pain and functional disability. Plain anteroposterior weight-bearing radiographs of both knees and musculoskeletal US of the more symptomatic knee were performed.

A. Impairment was assessed based on:

1. Clinical examination of the knee joint

Detailed clinical examination of the knee was done with stress on alignment, swelling (bony, soft tissue as Baker's cyst), tenderness (tested using Doyle Index) [15, 16], effusion, crepitus, and WOMAC OA index [17, 18] (was used to assess either knee pain by WOMAC pain subscale or knee stiffness by WOMAC stiffness subscale).

2. Radiological assessment of affected knee joint

Plain X-Ray of both knees in standing anteroposterior was done, and the radiological KOA severity was assessed by using the Kellgren-Lawrence (KL) global scale [19].

3. Sonographic assessment

Ultrasound of the knee was done to assess KOA severity and associated soft tissue abnormality [5]. The examination was performed by two rheumatologist ultrasonographers (ES S) and (AF Y) with high experience in musculoskeletal US using a 3–16-MHz linear array transducer (Samsung HS50, Korea). All settings were kept constant for each patient throughout the data collection except focus and image depth.

The subject was positioned supine with full flexion of the knee. Medial, sulcus, and lateral femoral articular cartilages were scanned in a transversal plane by proximal-distal probe sweeping over the anterior-central knee area to assess the cartilage of the femoral sulcus and the medial and lateral femoral condyles. The entire cartilage area reachable by US through the acoustic window was scanned. Cartilage was considered degenerated when loss of surface sharpness, increased inner echogenicity, local thinning, and/or total loss of cartilage thickness were observed. In a transverse plane and with the knees in maximum flexion, the femoral hyaline cartilage was assessed and classified in 5 degrees: 0, normal; 1, loss of normal sharpness level interfaces or increased echogenicity cartilage; 2A, modification from degree 1 with decreasing the cartilage thickness < 50% of his size; 2B, decreasing the cartilage thickness > 50%, but < 100%; and, 3, 100% local loss of cartilage thickness [20]. Then, the subject was asked to fully extend the knee, and medial and lateral femoral and tibial osteophytes as well as medial and lateral menisci were longitudinally imaged by anterior-posterior scanning from the medial and lateral side of the joint space and were subsequently evaluated for osteophyte presence and size using validated grading systems as follows: grade 0 = absence of osteophyte, grade 1 = minimal osteophyte, grade 2 = medium-sized osteophyte, and grade 3 = large osteophyte [21]. Meniscal extrusion was confirmed if it protruded > 3 mm perpendicularly from the joint line connecting the tibial and femoral bone ends [21].

B. Activity and participation

WOMAC score with the physical function subscale was used to assess the functional disability of the patients [18].

Statistical analysis

All statistical analyses were performed with IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) [22]. Continuous data were expressed as mean \pm SD, whereas categorical data were expressed in number and percentage. The differences between two groups or more were determined using independent sample Student's *t*-test or one-way analysis of variance test, respectively, for variables with continuous data or the χ^2 test for variables containing categorical data (χ^2) test ($P < 0.05$ was considered statistically significant). The Spearman correlation test was used to determine the correlation between two variables containing continuous data. Statistical significance was set at *p* less than 0.05.

Results

Sociodemographic, clinical, radiological, and ultrasonographic characteristics of the studied patients are illustrated in Tables 1 and 2. The mean age of the studied patients was 49.65 ± 6.84 years, and the majority of them were females (82.5%). According to KL grading, the largest percent of patients had grade II KOA (45%) followed by grade III (40%). Moreover, ultrasonographic GFC grading showed that 40% had grade 2b, followed by grade 2a in 30% of patients.

Correlations between clinical characteristics and either radiological or ultrasonographic findings of the studied patients are presented in Tables 3. The KL grading had significant positive correlations with age and disease duration as well as WOMAC scores ($p = <0.001$, <0.001 and <0.001 , respectively). Moreover, the GFC grading had significant

Table 1 Demographic and clinical characteristics of the studied patients

Data characteristics	
Gender	
Male, <i>n</i> (%)	7 (17.5)
Female, <i>n</i> (%)	33 (82.5)
Age (years) (mean ± SD)	49.65 ± 6.84
Disease duration (years) (mean ± SD)	6.60 ± 4.18
Height (cm)	163.17 ± 6.84
Weight (kg)	87.05 ± 11.66
BMI (kg/m²) (mean ± SD)	32.74 ± 3.88
Tenderness, <i>n</i> (%)	
No	2 (5)
Yes	38 (95)
Alignment, <i>n</i> (%)	
Normal	21 (52.5)
Varus	18 (45)
Valgus	1 (2.5)
Quadriceps muscle wasting, <i>n</i> (%)	
Yes	16 (40)
No	24 (60)
Range of motion, <i>n</i> (%)	
Full	27 (67.5)
Limited flexion	12 (30)
Limited extension	1 (2.5)
Stability, <i>n</i> (%)	
Stable	27 (67.5)
Lax	13 (32.5)
WOMAC pain subscale (mean ± SD)	8.80 ± 3.107
WOMAC stiffness subscale (mean ± SD)	2.00 ± 1.664
WOMAC function subscale (mean ± SD)	28.13 ± 11.062
WOMAC total score (mean ± SD)	38.83 ± 14.74

Table 2 Radiographic and US characteristics of the studied patients

Radiographic (KL) grade, <i>n</i> (%)	
I	3 (7.5)
II	18 (45)
III	16 (40)
IV	3 (7.5)
Ultrasonographic features, <i>n</i> (%)	
GFC grade	
1	7 (17.5)
2a	12 (30)
2b	16 (40)
3	5 (12.5)
Lateral osteophyte grading	
1	13 (32.5)
2	23 (57.5)
3	4 (10)
Medial osteophyte grading	
0	2 (5)
1	10 (25)
2	14 (35)
3	14 (35)
MME	
< 0.3	18 (45)
≥ 0.3	22 (55)
LME	
< 3 mm	28 (70)
≥ 3 mm	12 (30)
Effusion	
Yes	34 (85)
No	6 (15)
Baker's cyst	
Yes	11 (27.5)
No	29 (72.5)

SD standard deviation, *GFC* global femoral cartilage, *MME* medial meniscal extrusion, *LME* lateral meniscal extrusion

positive correlation with age, disease duration, and all WOMAC subscales (pain, stiffness, functional, and total $p = <0.001$, <0.001 , 0.040 , <0.001 , <0.001 , and <0.001). Significant positive correlations were found between other US parameters and all WOMAC subscales (pain, stiffness, functional, and total) except LME which was significantly correlated with WOMAC stiffness subscale only ($p = 0.018$).

Correlations between radiographic and ultrasonographic characteristics of KOA in the studied patients are illustrated in Table 4 and Figs. 1 and 2. There were significant positive correlations between KL grading and all US parameters.

Table 3 Correlation between clinical, radiological, and ultrasonographic parameters

	K-L <i>r</i> (<i>P</i>)	GFC <i>r</i> (<i>P</i>)	MME <i>r</i> (<i>P</i>)	LME <i>r</i> (<i>P</i>)	Med. osteophyte <i>r</i> (<i>P</i>)	Lat. osteophyte <i>r</i> (<i>P</i>)
WOMAC pain	0.456 (0.003*)	0.327 (0.040*)	0.386 (0.014*)	0.287 (0.073)	0.352 (0.026*)	0.441 (0.004*)
WOMAC stiffness	0.641 (< 0.001*)	0.558 (< 0.001*)	0.390 (0.013*)	0.374 (0.018*)	0.457 (0.003*)	0.452 (0.003*)
WOMAC function	0.732 (< 0.001*)	0.615 (< 0.001*)	0.430 (0.006*)	0.172 (0.290)	0.562 (< 0.001*)	0.568 (< 0.001*)
WOMAC total score	0.736 (< 0.001*)	0.607 (< 0.001*)	0.413 (0.008*)	0.202 (0.211)	0.541 (< 0.001*)	0.573 (< 0.001*)

WOMAC score Western Ontario and McMaster Universities Osteoarthritis score, GFC global femoral cartilage, MME medial meniscal extrusion, LME lateral meniscal extrusion, *r* Spearman's correlation, *p* *p* value for comparing between the studied groups

*Statistically significant at $p \leq 0.05$

Table 4 Correlation between radiological and ultrasound parameters

Ultrasound features	KL grading score	
	<i>R</i>	(<i>p</i>)
GFC	0.794	< 0.001*
MME	0.504	0.001*
LME	0.320	0.044*
Med. osteophyte grading	0.632	< 0.001*
Lat. osteophyte grading	0.614	< 0.001*

GFC global femoral cartilage, MME medial meniscal extrusion, LME lateral meniscal extrusion. *p* *p* value for comparing between the studied groups

*Statistically significant at $p \leq 0.05$

Discussion

Cartilage breakdown, subchondral bone alterations, and formation of osteophytes are the key points in the natural development (cascade) of KOA, with pain and loss of function counting as major devastating consequences [23]. Hence, sensitive tools for their development and progression are mandatory. Conventional radiography has long been the major tool for assessment of KOA; however, it is an imprecise guide to the likelihood that knee pain or disability will be present especially in the early and mild cases [24]. Several studies have argued against the association between radiographic grading of KOA and pain severity and function as assessed by WOMAC. Other studies [25–27] found no correlation between radiographic grading and neither functional status using Modified Lower Extremity Functional Scale nor disability as assessed by the Health Assessment Questionnaire (HAQ) or WOMAC score. Even the radiographic osteophyte length was not correlated with pain severity in another study by Creamer et al. [28]. On the other hand, Muraki et al. [29] found a strong association between knee pain and radiological joint space narrowing. These inconsistent results across studies elucidate that conventional radiography may fail to detect structural changes associated with pain in early KOA, especially with patients of mild to moderate severity. It does

Table 5 Multivariate linear regression analysis for the ultrasonographic parameters affecting WOMAC total score and WOMAC subscores

	Multivariate			
	Sig.	<i>B</i>	<i>SE</i>	<i>T</i>
WOMAC total score				
GFC	0.004	7.591	2.489	3.049
Med. osteophyte	0.087	4.356	2.477	1.758
LME	0.928	− 1.163	12.719	− 0.091
$R^2 = 0.445$				
$F = 9.628, p = < 0.001^*$				
WOMAC stiffness score				
GFC	0.020	0.730	0.300	2.431
Med. osteophyte	0.402	0.254	0.299	0.849
LME	0.164	2.182	1.535	1.422
$R^2 = 0.366$				
$F = 6.932, p = 0.001^*$				
WOMAC physical function score				
GFC	0.003*	5.978	1.865	3.206
Med. osteophyte	3.294	0.084	1.855	1.776
LME	− 6.529	0.498	9.527	− 0.685
$R^2 = 0.447$				
$F = 9.704, p = < 0.001^*$				
WOMAC pain score				
GFC	0.149	0.885	0.885	1.473
Med. osteophyte	0.187	0.805	0.805	1.346
LME	0.301	3.219	3.219	1.049
$R^2 = 0.272$				
$F = 4.494, p = 0.009^*$				

*Statistically significant at $p \leq 0.05$

WOMAC score Western Ontario and McMaster Universities Osteoarthritis score, GFC global femoral cartilage, MME medial meniscal extrusion, LME lateral meniscal extrusion

not adequately depict articular cartilage and other soft tissue damage that patients mostly categorize [30].

Since then more research has been conducted on tools more accurately depicting early cartilage and soft tissue damage as MRI and US. Since MRI is an

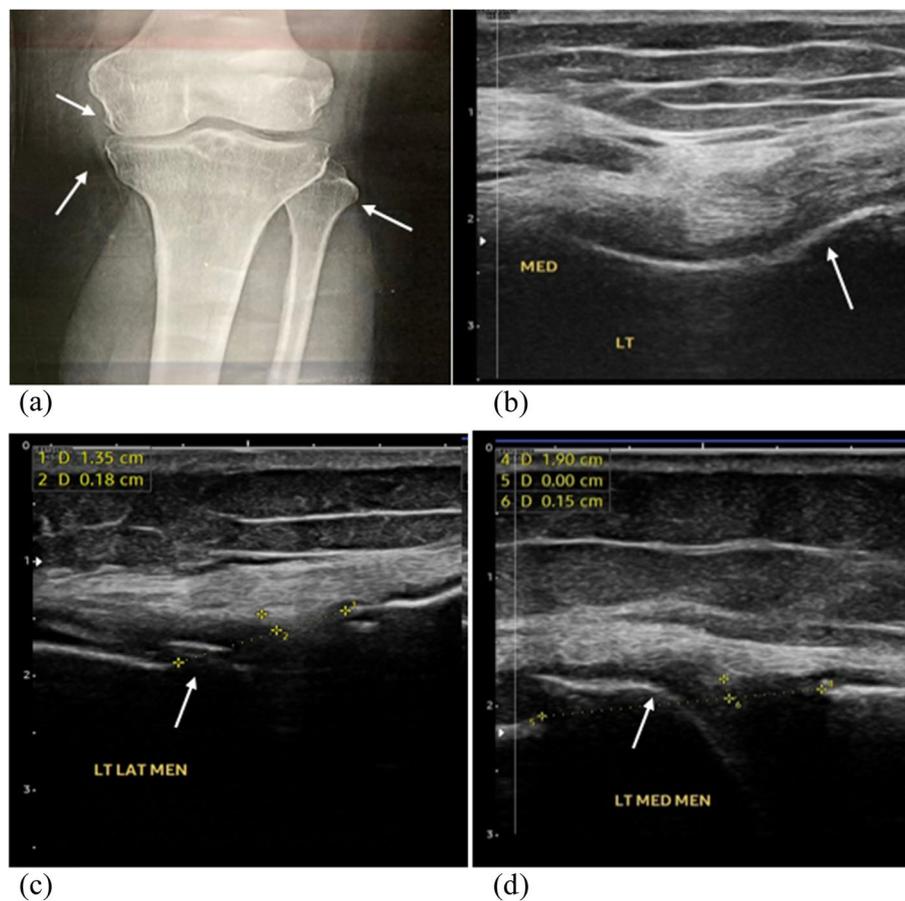


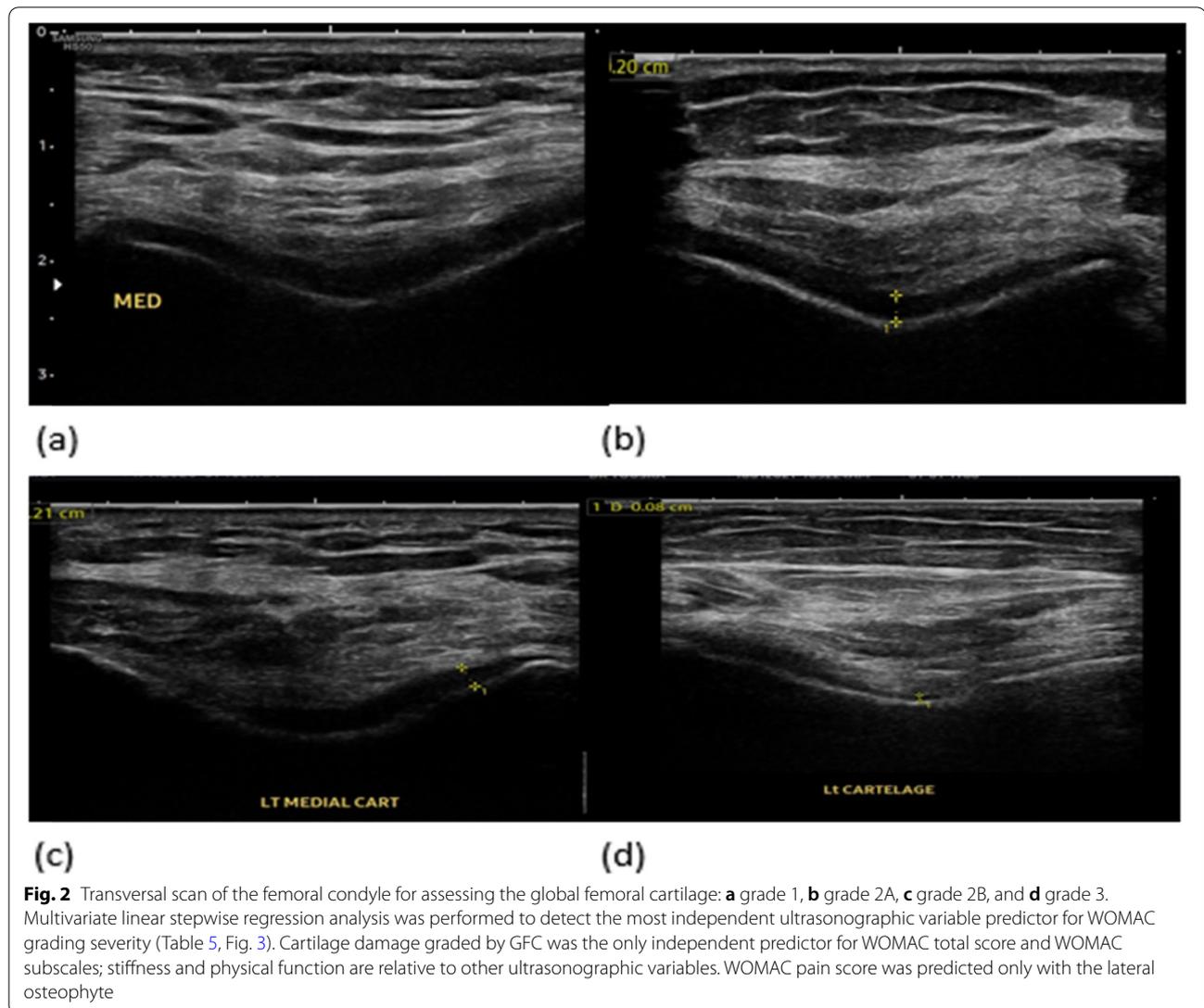
Fig. 1 **a** Plain X-ray of left knee joint anteroposterior 48years old female patient showing grade 2 KL grading with presence of definite osteophytes and possible joint space narrowing. Sonographic assessment showed **b** global femoral cartilage (GFC) semi-quantitative grading G2b with loss of normal cartilage interfaces sharpness and increased echogenicity of the cartilage together with local thinning (> 50% but < 100% of the cartilage), **c** lateral medium osteophyte grade 2 and lateral meniscal extrusion measuring 1.8 mm, and **d** medial large osteophyte grade 3 and medial meniscal extrusion measuring 1.5 mm

expensive tool, and not readily available in any clinical setting, more effort was invested with US and its capability in defining those early soft tissue changes in KOA especially the ones related to pain and eventually leading to loss of function as concluded by Abicalaf et al. [31]. Recently ultrasound has become popular among rheumatologists as the first-choice imaging for the evaluation and monitoring of KOA.

To evaluate the ability of US in assessing severity of KOA, we measured US GFC grade and lateral and medial osteophyte grade as well as medial and lateral meniscal extrusion together with radiographic KL grading. Significant correlation was found between radiographic KL grading and pain and function as assessed by WOMAC score, as well as between radiographic KL grading and all US findings which was of moderate strength with all sonographic parameters, except for GFC which was of high strength ($r > 0.75$). Also, a study of Mortada et al.

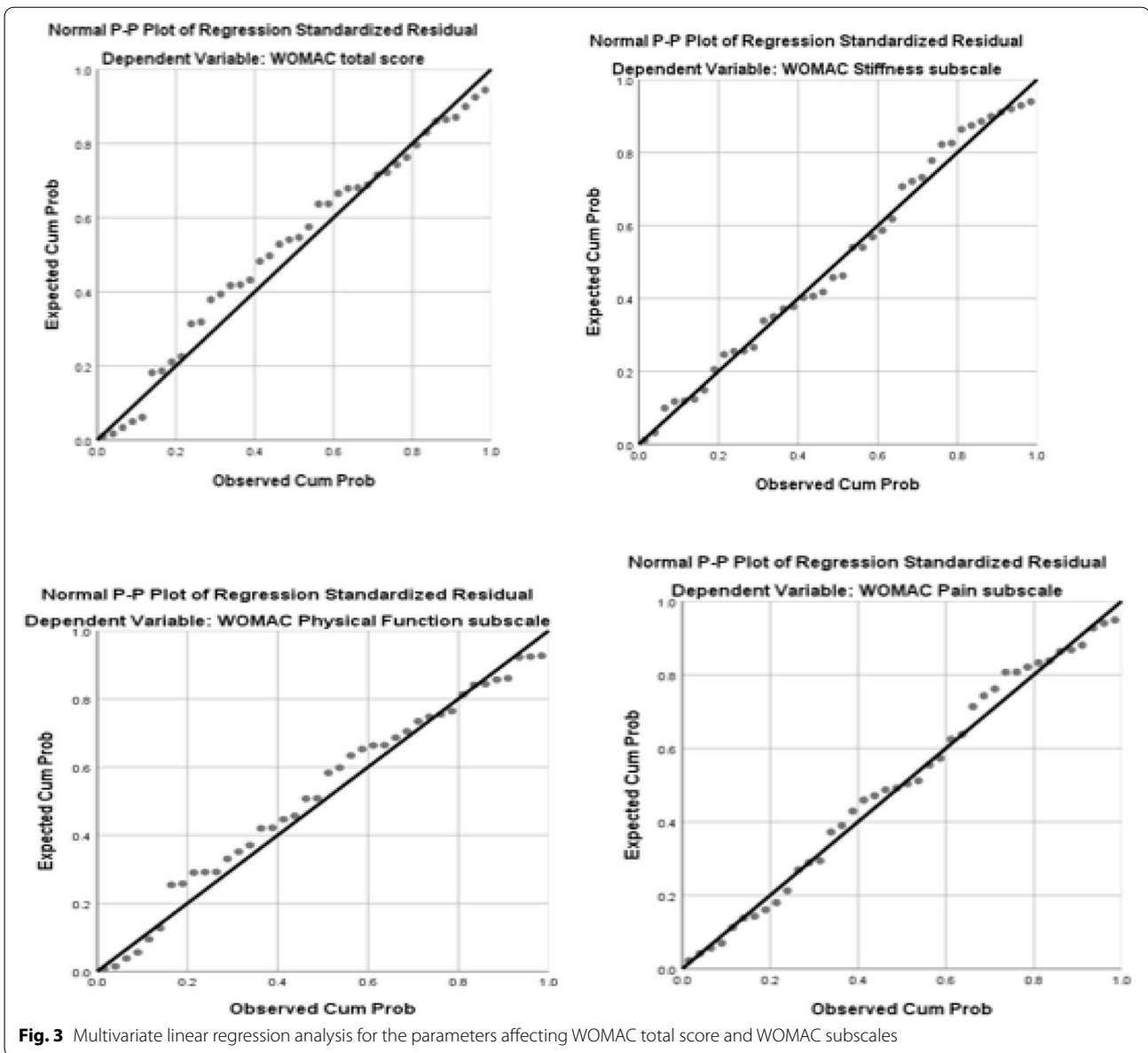
[32] found good agreement between KL grading scale and a proposed simple and reliable US grading scale based on medial osteophytic grading. Interestingly, Malas et al. in 2014 [33] reported that a positive correlation was discovered between US meniscal extrusion measurements and radiological KL grade. This was also reported by Brom et al. [34] concluding that US is a valid method with high sensitivity and specificity for detecting radiographic KOA.

As for correlation between US parameters and WOMAC scores of pain and function, there was also significant correlation with all US findings including GFC, MME, and medial and lateral osteophyte grading except LME which was only correlated with WOMAC stiffness subscale. To detect the most independent ultrasonographic variables predictors for WOMAC grading severity, multivariate linear regression analysis was performed. Cartilage damage graded by GFC was the only



independent predictor for WOMAC total score and WOMAC subscales; stiffness and physical function are relative to other ultrasonographic variables. On the other hand, lateral osteophyte grading was the only predictor of WOMAC pain score. This finding is supported by the fact that hyaline cartilage has not got pain fibers and so cannot be the source of pain [28], while growing osteophytes show neovascularization, which can be accompanied by sensory nerve growth and therefore be connected to pain generation [35]. In addition to this, osteophyte stimulation of sensory nerve terminals in the neighboring synovium can also induce bone-related pain [36]. In a study by Serban et al. [27], they reported that cartilage damage score was an independent predictor for both VAS and WOMAC scores. Medial osteophytes were associated with pain at palpation and are independent predictors for the WOMAC score. Lateral meniscal protrusion was

also a predictor for the WOMAC score. Interestingly, Mortada et al. reported that the medial femoral osteophyte, which represents the degenerative domain of the novel proposed ultrasonographic ZAGAZIG scale, was well correlated with WOMAC subscales (pain, stiffness and function) [37]. Also, Chen et al. [38] found that the cartilage damage on US was linked to worse WOMAC and Lequesne index scores. Also, Kijima et al. [39] found that the amount of MME was correlated to pain intensity. Our results was also supported by Podlipská et al. in 2017 [21] who reported that early cartilage changes seen in US lead to pain in KOA, but in contrast to our results, they found no significant association with meniscal extrusion suggesting that the extruded meniscus was simply a coexisting OA feature rather than painful and disabling pathological processes within the knee in symptomatic patients. Similarly, Razek et al. in 2016 [40] reported that



US characteristics of cartilage damage, osteophytes, and synovial effusion were related to poorer WOMAC scores. On the contrary, Malas et al. [33] did not find a positive association between WOMAC scales and the severity of cartilage damage.

This study has some limitations. Firstly, with a small sample size, more researches on a large number of patients are needed to determine the validity of this study. Second, the lack of data on the patients' treatment is one of the study's significant limitations: chronic use of anti-inflammatories or analgesics can alter pain perception. Third, we did not compare our findings to those of a control group (asymptomatic with radiographic OA). Fourth,

ultrasonography assessment measures were conducted only once by one reader. Fifth is the lack of comparison of US findings with MRI findings, as we did not regard the presence of bone marrow lesions as a significant source of pain in KOA. The link between KOA symptoms and US findings is still unclear and contentious, and it has to be investigated further in larger research.

Conclusions

GFC was the only independent predictor for WOMAC loss of function, and lateral osteophyte grading was the only predictor for WOMAC pain score. US can visualize multiple aspects of the joint and was significantly

correlated in this study with radiographic assessment, and by time, radiography may not be the method of choice.

Abbreviations

OA: Osteoarthritis; KOA: Knee osteoarthritis; K-L: Kellgren-Lawrence (K-L) scale; US: Ultrasound; GFC: Global femoral hyaline cartilage; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index scale; CR: Conventional radiography; ICF: International Classification of Functioning, Disability and Health; MME: Medial meniscal extrusion; LME: Lateral meniscal extrusion; VAS: Visual analog scale.

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Authors' contributions

ES S performed the sonographic assessment and contributed to the interpretation of data and work edit. AM M put the idea, design of the work, and general supervision on the whole work. E R performed the interpretation of data and work edit. T R performed the routine investigations assessment and participated in revising and editing the work. WF N contributed to the clinical assessment, interpretation of data, and writing of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The local Ethics Committee of Faculty of Medicine, Alexandria University, Egypt (IRB NO: 00012098-FWA NO: 00018699), approved the study. Date of approval: 16 July 2020. Serial number: 0201371. Informed consent was obtained from every patient.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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