Western Ontario and McMaster Universities Arthritis Index (WOMAC) Optimal Value in Diagnosing Fibromyalgia: Report from a Multivariate Study on Patients with Knee osteoarthritis

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Abstract

Background:
Fibromyalgia (FM) and osteoarthritis (OA) share common clinical properties and pathologic etiologies. In the current study we aim to assess the prevalence of overlapping FM in a population of knee OA patients and to evaluate the diagnostic performance of Western Ontario Macmaster (WOMAC) for FM in OA patients.

Methods:
In a single-center observational study we recruited a consecutive sample of 100 knee osteoarthritis. The OA patients were assessed for pain, stiffness and function using WOMAC and for possible FM diagnosis using ACR 2010 diagnostic criteria. In order to find independent predictors for fibromyalgia diagnosis, univariate and multivariate logistic regression analyses were utilized. The results regression analysis was used to build the final prediction model. Receiver-operating characteristic (ROC) curves and Youden's J index were used to identify the best cutoff values for predictor parameters of fibromyalgia.

Results:
In a population of 100 OA patients in this study, 41 had fibromyalgia based on ACR criteria. Age (mean of 55.43±8.94 vs. 51.4±8.59; P= 0.025), BMI (25.17±3.52 vs. 23.59 ±3.77; P= 0.03) and WOMAC score (46.19±14.10 vs. 35.69±11.19; P= <0.001) were significantly higher in patients with FM than patients without FM. Univariate analysis identified that the age, BMI and WOMAC score (Ps= 0.029, 0.041, and <0.001, respectively) are significantly associated with FM diagnosis. In multivariate analysis, WOMAC score (OR: 0.93 (95% CI 0.90–0.97), P< 0.001) was identified as independent predictors for diagnosis of FM. Using Receiving operator curve, the Area under the curve (AUC) of WOMAC score was 0.715 (95%CI: 0.614-0.817) and the optimum cutoff point for WOMAC score for diagnosis of FM was 43.5.

Conclusion:
It is concluded from this study that WOMAC scores > 43.5 are useful for suggesting FM as a secondary diagnosis in knee OA patients. Future studies are necessary to establish the results of the current study in a more general context, given the limited available evidence.

Introduction
Osteoarthritis (OA) is the most prevalent chronic joint illness in elderly adults and is characterized by pain and disability caused by joint inflammation and degradation (Staud, 2011). Fibromyalgia (FM) is a musculoskeletal and connective tissue disorder (Häuser & Henningsen, 2014) characterized by persistent widespread pain, sleep problems, exhaustion, and a broad variety of other physical and psychological symptoms (Häuser et al., 2015; Kroenke, 2014). Estimates place the frequency of FM in the general population between 0.7–9.3%, with a higher prevalence among women and the elderly (Häuser et al., 2015). FM impacts the quality of life (QOL) of patients to a degree equivalent to that of blindness and renal failure (Brazier et al., 2004).

FM and OA share common pain mechanisms(Staud, 2011), and also there is a correlation between disease activity between these two disorders(Haliloglu et al., 2014). Previous studies show that the FM is found in between 7–11% of patients with OA(Hawker et al., 2010; Lavín, 2001).

There are no diagnostic biomarkers or para-clinical procedures for FM, and the updated 2010 American college of rheumatology (ACR) criteria and the clinical judgment of the rheumatologists are now used for diagnosis (Häuser et al., 2015). The ACR criteria are determined by the sum of two indices: the widespread pain index (WPI) and the symptom severity score (SSS) (Wolfe et al., 2010). The Western Ontario Macmaster (WOMAC) is a validated health status tool for
assessing pain and functioning in knee or hip osteoarthritis patients (Bellamy et al., 1988). The WOMAC's capacity to detect pain and function correlates with fibromyalgia (FM) evaluations and is recognized as a valuable adjunct instrument for examining FM patients (Wolfe, 1999).

The aim of this study is to assess the diagnostic utility of WOMAC scores in patients with both OA and FM. In this study, we will examine the possibility that WOMAC score can be used to classify OA patients who may also be diagnosed with FM.

Methods

Study design and participants

This cross-sectional, single-center observational study was carried out at the Beheshti Hospital in Qom, Iran, between January 2020 and December 2021. All referred patients to the rheumatology clinic of Beheshti hospital were evaluated for eligibility of participation in the study. The Qom University of Medical Sciences ethics committee has approved the study protocols, which were designed in accordance with the statement on strengthening the reporting of observational studies in epidemiology (STROBE). Signed informed consent was obtained from each study participant. The study was conducted in accordance with the Helsinki Declaration principles.

We recruited a consecutive sample of patients who had diagnosed with knee osteoarthritis from the Beheshti hospital rheumatologic clinic. Knee osteoarthritis was diagnosed based on symptoms such as joint pain and radiological findings with opinion of a rheumatologist. Patients with other autoimmune diseases, endocrine disorders, chronic hepatic or renal disease and malignancies, were excluded. Diagnosis of fibromyalgia were made based on ACR 1990 classification criteria and ACR 2010 diagnostic criteria for fibromyalgia(Wolfe et al., 2010).

Patient's demographic including age (year), gender, BMI, marital (married/ not married), and employment (employed/non-employed) status were recorded. Laboratory findings including white blood cell (WBC-cell/mm3), erythrocyte sedimentation rate (ESR) (mm/hr), C-reactive protein (CRP) (mg/L), thyroid-stimulating hormone (TSH) (mIU/L), free triiodothyronine (FT3) (ng/dL), free thyroxine (FT4) (ng/dL), Rheumatoid factor (RF) (IU/mL), Anti–cyclic citrullinated peptide (anti-CCP) antibody (EU/mL), fluorescent antinuclear antibody (FANA) (positive/negative), Calcium (Ca) (mg/dL), phosphorus (Ph) (mg/dL), Parathyroid hormone (PTH) (pg/mL), 1,25-dihydroxvitamin D (1,25-D) (pg/mL) were recruited. Based on the cut-off value of the laboratory where the tests were studied, ESR (mm/hr), CRP (mg/L), RF (IU/mL), and anti-CCP (EU/mL) values were accepted as positive or negative. Values above 22 mm/hr in men and 29 mm/hr in women for ESR, values above 10 mg/L for CRP, values above 20 IU/mL for RF, and values above 5 U/mL for anti-CCP were accepted as positive.

Measures

Fibromyalgia diagnosis and severity assessment

We used the Widespread Pain Index (WPI), and the Symptom Severity Scale (SSS), according to the 2010 modified ACR criteria for Fibromyalgia(Wolfe et al., 2010). The WPI quantifies the extent of bodily pain on a 0–19 scale during the last week and the SSS is a 0–12 measure of symptom severity that includes cognitive symptoms, fatigue, feeling unrefreshed upon waking. Total FM severity scores were calculated by summing WPI and SSS scores. Patients diagnosed with fibromyalgia according to 2010 ACR criteria based on WPI and SSS scores.

The Western Ontario MacMaster osteoarthritis questionnaire (WOMAC)

WOMAC assess pain, stiffness, and function of the lower extremity, it is a 24–item, self-report questionnaire consisting of three subscales: 17 questions on physical function, 5 questions on pain, and 2 questions on stiffness. Each query has five response options including: 0, none; 1, mild; 2, moderate; 3, severe; and 4, extreme The subscale scores can vary as follows:
pain, 0–20; stiffness, 0–8, and physical function, 0–68. Total WOMAC scores were defined as the unweighted sums of all 24 items and ranged from 0 to 96. Lower scores represent less pain, less stiffness, and greater levels of functional status.

Statistics

We used SPSS (Windows ver. 18; IBM SPSS Inc.) for our analysis. Presentation descriptive data in mean, SD, frequency, and percentage. The Kolmogorov-Smirnov test was used to assess the normality of the data. We obtained an Independent Sample t test for continuous variables with normal distribution, the Mann-Whitney U test for continuous non-normal variables, and a Chi-square or fisher’s exact test for nominal variables. In order to find independent predictors for fibromyalgia diagnosis, univariate and multivariate logistic regression analyses were utilized. The results of the multivariate (backward stepwise) logistic regression analysis were used to build the final prediction model. Receiver-operating characteristic (ROC) curves and Youden’s J index were used to identify the best cutoff values for the most of important parameter for the diagnosis of fibromyalgia. All p values less than 0.05 were considered statistically significant.

Results

One hundred knee osteoarthritis patients recruited in the study, of whom 41 patients had fibromyalgia. The mean (SD) age and BMI of all participants were 53.06 (8.92) and 24.24, respectively, and 98 (98%) of all patients were female. Age (mean of 55.43 ± 8.94 vs. 51.4 ± 8.59; P = 0.025), BMI (25.17 ± 3.52 vs. 23.59 ± 3.77; P = 0.03) and WOMAC score (46.19 ± 14.10 vs. 35.69 ± 11.19; P = < 0.001) were significantly higher in patients with fibromyalgia. Demographic and laboratory findings of patients with or without fibromyalgia are presented in (Table 1).
### Table 1: Demographic, and laboratory findings of patients with or without fibromyalgia

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total patients</th>
<th>Patients With fibromyalgia (N = 41)</th>
<th>Patients Without fibromyalgia (N = 59)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, years (SD)</td>
<td>53.06 (8.92)</td>
<td>55.43 (8.94)</td>
<td>51.4 (8.59)</td>
<td>0.025*</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>2 (2%)</td>
<td>2 (4.9%)</td>
<td>0 (0%)</td>
<td>0.87</td>
</tr>
<tr>
<td>Female</td>
<td>98 (98%)</td>
<td>39 (95.1)</td>
<td>59 (100%)</td>
<td></td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Married</td>
<td>98 (98%)</td>
<td>39</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>Employment status</td>
<td></td>
<td></td>
<td></td>
<td>0.10</td>
</tr>
<tr>
<td>Employed</td>
<td>89 (89%)</td>
<td>34</td>
<td>55</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>24.24 (3.73)</td>
<td>25.17 (3.52)</td>
<td>23.59 (3.77)</td>
<td>0.03*</td>
</tr>
<tr>
<td><strong>Laboratory findings</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WBC</td>
<td>6.87 (1.99)</td>
<td>7.01 (2.44)</td>
<td>6.77 (1.62)</td>
<td>0.55</td>
</tr>
<tr>
<td>ESR (positive)</td>
<td>22 (22%)</td>
<td>8</td>
<td>14</td>
<td>0.59</td>
</tr>
<tr>
<td>CRP (positive)</td>
<td>9 (9%)</td>
<td>4</td>
<td>5</td>
<td>0.83</td>
</tr>
<tr>
<td>TSH</td>
<td>2.92 (1.86)</td>
<td>2.99 (2.09)</td>
<td>2.86 (1.7)</td>
<td>0.73</td>
</tr>
<tr>
<td>FT3</td>
<td>1.53 (0.83)</td>
<td>1.47 (0.84)</td>
<td>1.58 (0.83)</td>
<td>0.52</td>
</tr>
<tr>
<td>FT4</td>
<td>1.62 (1.65)</td>
<td>1.61 (1.33)</td>
<td>1.63 (1.87)</td>
<td>0.95</td>
</tr>
<tr>
<td>RF (positive)</td>
<td>1 (1%)</td>
<td>0</td>
<td>1</td>
<td>0.40</td>
</tr>
<tr>
<td>anti-CCP (positive)</td>
<td></td>
<td>0</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>FANA (positive)</td>
<td>13 (13%)</td>
<td>6</td>
<td>7</td>
<td>0.69</td>
</tr>
<tr>
<td>Ca</td>
<td>9.30 (0.56)</td>
<td>9.28 (0.54)</td>
<td>9.31 (0.57)</td>
<td>0.75</td>
</tr>
<tr>
<td>Ph</td>
<td>3.76 (0.55)</td>
<td>3.87 (0.57)</td>
<td>3.68 (0.53)</td>
<td>0.09</td>
</tr>
<tr>
<td>PTH</td>
<td>44.39 (16.58)</td>
<td>44.24 (18.51)</td>
<td>44.49 (15.21)</td>
<td>0.94</td>
</tr>
<tr>
<td>1,25- vitamin D</td>
<td>40.25 (21.17)</td>
<td>42.38 (20.89)</td>
<td>38.76 (21.42)</td>
<td>0.40</td>
</tr>
<tr>
<td>WOMAC score</td>
<td>40 (13.44)</td>
<td>46.19 (14.10)</td>
<td>35.69 (11.19)</td>
<td>&lt; 0.001*</td>
</tr>
</tbody>
</table>

BMI = Body mass index, Ca = calcium, CRP = C reactive protein, ESR = Erythrocyte sedimentation rate, FANA = fluorescent antinuclear antibody, FT3 = Free T3, FT4 = Free T4, Ph = phosphorous, PTH = Parathyroid hormone, RF = Rheumatoid factor, SD = Standard Deviation, TSH = Thyroid stimulating hormone, WBC = White blood cells count, WOMAC = Western Ontario and McMaster Universities Arthritis Index

As shown in (Table 2), Univariate analysis identified that the age, BMI and WOMAC score (Ps = 0.029, 0.041, and < 0.001, respectively) acted as predictors for diagnosis of fibromyalgia. In multivariate analysis, WOMAC score (OR: 0.93 (95% CI 0.90–0.97), P < 0.001) was identified as independent predictors for diagnosis of fibromyalgia.
Table 2
Univariate and multivariate analyses for diagnosis of fibromyalgia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (CI 95%)</td>
<td>P-Value</td>
</tr>
<tr>
<td>Age</td>
<td>0.94 (0.90–0.99)</td>
<td>0.029*</td>
</tr>
<tr>
<td>BMI</td>
<td>0.88 (0.79–0.99)</td>
<td>0.041*</td>
</tr>
<tr>
<td>WOMAC score</td>
<td>0.93 (0.9–0.97)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

BMI, Body mass index, CI = Confidence interval, OR = Odds ratio, WOMAC = Western Ontario and McMaster Universities Arthritis Index

The ROC curve analysis results for the ability of WOMAC score for diagnosis of fibromyalgia is shown in (Table 3) and (Fig. 1). The AUC of WOMAC score was 0.715 (95%CI: 0.614–0.817) and the optimum cutoff point for WOMAC score for diagnosis of fibromyalgia was 43.5.

Table 3
Predictive performance of WOMAC score for diagnosing fibromyalgia

<table>
<thead>
<tr>
<th>Variable</th>
<th>AUC (95%CI)</th>
<th>P-Value</th>
<th>Youden's index (%)</th>
<th>Optimum cutoff value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WOMAC score</td>
<td>0.715 (0.614–0.817)</td>
<td>&lt; 0.001</td>
<td>0.341</td>
<td>43.5</td>
<td>56.1</td>
<td>78</td>
<td>63.89%</td>
<td>71.88%</td>
<td>69%</td>
</tr>
</tbody>
</table>

AUC = Area under the curve, NPV = Negative predictive value, PPV = Positive predictive value, WOMAC = Western Ontario and McMaster Universities Arthritis Index

Discussion

In the present research, 41% of patients with knee OA were diagnosed with overlapping FM. FM and OA patients were older and had a greater BMI and WOMAC score than OA patients. In the univariate analysis, BMI and WOMAC score are associated to the diagnosis of FM in OA patients. Multivariate study and ROC analysis demonstrated that a WOMAC score > 43.5 had a high degree of sensitivity and specificity for classifying FM patients.

WOMAC was developed primarily to measure pain, stiffness, and function in osteoarthritis patients, but it has been shown to measure more than just OA-related impairments. In a longitudinal study of osteoarthritis (OA), fibromyalgia (FM), and rheumatoid arthritis (RA), WOMAC was shown to have a substantial correlation with the number of symptoms, exhaustion, and depression, which are symptomatic of the mental and physical condition of the subjects (Wolfe, 1999). Since the WOMAC score has a good link with the pain and function scores in FM, it may be helpful as a supplementary diagnostic test for FM in patients with lower extremity symptoms (such as knee osteoarthritis) (Wolfe, 1999). Notably, in a clinical study of individuals with Knee osteoarthritis, the WOMAC score was considerably higher in patients with clinical depression than in patients without clinical depression; Beck Depression Inventory (BDI) was used to quantify depression (Yilmaz et al., 2015).

The intensity of FM symptoms, particularly pain, is related to a higher WOMAC score in the afflicted joint, according to a subsequent research of preoperative knee OA patients. In this research, patients with a high FM score (according to ACR criteria) had substantially higher WOMAC ratings on all three pain, stiffness, and function subscales than those with a moderate or low FM score (Brummett et al., 2015). The results of a research including 655 knee or hip OA patients and 537 FM patients indicated that the WOMAC had a strong performance, excellent fit, and acceptable scaling, with a slightly
improved pain assessment in OA than in FM (Wolfe & Kong, 1999). Dimensions of WOMAC are fundamental to OA, and they also play an instrumental role in FM diagnosis (Wolfe & Kong, 1999).

FM and OA have comparable pathologic etiologies of pain, including inadequate descending regulation of pain and central sensitization (Staud, 2011). According to our findings, when OA patients are checked for FM characteristics, the proportion of patients with an overlapping FM diagnosis may be more than anticipated. There is a paucity of evidence in the scientific literature on a deeper understanding of how FM manifests in other rheumatologic disorders, such as OA. Consequently, our study’s findings are accompanied by two primary key points: Firstly, despite the fact that OA patients may have persistent widespread pain, a number of symptoms are often overlooked owing to the main diagnosis of OA. The incidence of 7 to 11% of FM diagnoses in OA patients in the past is reflective of this concern (Hawker et al., 2010; Lavín, 2001). In our study, 41% of knee OA patients can be classified as overlapping FM according to ACR criteria; Second, the data from prior research on the link between pain mechanisms, symptom intensity, and constitutional status of FM and OA shows that when OA is diagnosed (particularly when not all symptoms are explicable by OA), FM should be considered as an alternative explanation. Considering our findings on the performance of WOMAC compared to ACR criteria in diagnosing FM and the evidence described above, we propose that, while not all OA patients are necessarily diagnosed with FM, OA patients with particular WOMAC scores may benefit a subsequent assessment in search of FM.

Conclusion

It is concluded from this study that WOMAC scores > 43.5 are useful for suggesting FM as a secondary diagnosis in knee OA patients. Future studies are necessary to establish the results of the current study in a more general context, given the limited available evidence.

Declarations

Acknowledgments:

None.

Sources of funding:

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest statement of all authors:

The authors declare no conflict of interest.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Informed consent was obtained from each study participant. The study was conducted in accordance with the Helsinki Declaration principles and was approved by the Shahid Beheshti hospital ethics committee.

CONSENT TO PUBLISH

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

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

COMPETING INTERESTS
The authors of this article declare no competing interests.

FUNDING

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AUTHORS CONTRIBUTIONS

All authors contributed equally.

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References

Figures

Figure 1

ROC curve for diagnosis of fibromyalgia with WOMAC score; WOMAC score had an AUC of 0.715.