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Original Article

Malnutrition Diagnosis in Outpatients with Knee Osteoarthritis: A Hospital-based Case-Control Study in Iranian Population

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ABSTRACT

Background and Objectives: Knee osteoarthritis is a musculoskeletal disorder. In this case-control study, associations of knee osteoarthritis outcomes with nutritional status were assessed in patients with knee osteoarthritis and non-knee osteoarthritis participants.

Materials and Methods: Mini-nutritional assessment questionnaire was used to assess the nutritional status. Osteoarthritis outcome score-patellofemoral questionnaire was used to assess the pain, stiffness and quality of life score associated with knee osteoarthritis.

Results: Patients with knee osteoarthritis showed higher malnutrition index scores (P = 0.001) and malnutrition rates (10% against 2%, P = 0.003) than those non-knee osteoarthritis participants did. In knee osteoarthritis patients, a significant positive association was detected between the scores of the malnutrition index and the quality of life subscale (P = 0.036; r = 0.297; CI: 0.045, 0.549). Patients with normal nutritional status were at lower risks of knee osteoarthritis than those malnourished participants were after adjusting for age, sex and body mass index (P = 0.019).

Conclusions: Regarding increasing prevalence of knee osteoarthritis and malnutrition, especially in the elderly population, a preventive assessment for knee osteoarthritis includes further attentions to the nutritional status of this population.

Keywords: Knee osteoarthritis, Malnutrition, Body mass index, Knee joint, Nutritional status

Highlights

- Prevalence of malnutrition was higher knee-osteoarthritis patients than non-knee osteoarthritis people.
- Normal nutritional status is associated with a lower risk of knee osteoarthritis.
- Adequate nutritional status leads to a lower risk of suffering from pains.
- A better nutritional status is associated with a higher quality of life in knee osteoarthritis patients.

Introduction

Osteoarthritis (OA) is the most common joint disease that manifests itself in mobile joints by destructing articular cartilage with new ossification on the surface and margins of the joint (1). The OA of the joints constitutes more than 80% of the problems of people over 65 years old (2). Knee osteoarthritis (KOA) is a type of musculoskeletal disorder that affects primarily older people, causing pain and physical disability. It affects people's social participation and quality of life (QOL) (3). It is estimated that KOA accounts for nearly 4/5 of the burden of OA worldwide and its prevalence increases with increases in weight (obesity) and age (4). Patellofemoral pain accounts for 25 to 40% of knee problems (5). It usually occurs around the kneecap and is aggravated by squatting, climbing and other activities such as running (6). Patellofemoral pain may be part of a degenerative joint disorders in middle-aged and older people with

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patellofemoral osteoarthritis (1). Several risk factors are involved in the development and progression of OA, which can be divided into personal characteristics (e.g. age, sex, overweight and obesity, family history and diet) and joint factors (e.g. injury, joint malalignment and abnormal loading of the joints) that interact in complex circumstances (7).

Arthritis management includes education, physical therapy, diet, exercise intervention, weight loss and surgery (8). Use of nonsteroidal anti-inflammatory drugs, including diclofenac sodium, celecoxib, meloxicam and naproxen as well as paracetamol, decreases pain or alleviates joint swelling (9). As a risk factor and management strategy, the relationship between diet and OA has been focused. Low intake of certain nutrients such as vitamins D, E and K and magnesium has been accompanied by an increased risks of developing osteoarthritis or worsening symptoms (10-14). In contrast, higher levels of circulating vitamins C and E did not protect against incident radiographic KOA and may be linked to an increased risk of KOA (15). In contrast, prospective cohort studies and randomized controlled trials of mono-nutrient supplementation of vitamins C, D, E and K have shown no protective effects for OA (16-21). Moreover, it has been shown that addressing nutritional status before arthroplasty may decrease the risk of adverse outcomes (22). These suggest that focusing on individual nutrients may be insufficient and the effects of food groups and overall dietary patterns should be considered when studying the diet-disease relationships. Moreover, overweight and obesity are other risk factors for OA. Obesity increases the load on the weight-bearing joints and cartilage and contributes to their degradation (23). Approximately 70% of OA can be prevented by avoiding excess weight gains and joint damages (9).

Knee injury and osteoarthritis outcome score-patellofemoral (KOOS-PF) is a subjective questionnaire developed to estimate the short and long-term symptoms and function in patients with KOA (24). Mini-nutritional assessment (MNA) is a valuable diagnostic tool with a standardized scoring system for identifying elderly patients, who are at risk from malnutrition and those already malnourished in clinical settings (25). This questionnaire has been translated into several languages and is used in clinics worldwide (26). Therefore, assessment of nutritional status is an essential method for appropriate management and prevention of OA (27).

Studies show that patients with rheumatoid arthritis (RA) are susceptible to malnutrition as their drugs often affect appetite as well as absorption and digestion of nutrients. Furthermore, joint pain and fatigue make patients experience difficulty buying and preparing foods (28). In addition, inflammation may intensify nutritional needs (29). However, a few studies have investigated the relationship between malnutrition and the risk of KOA and its subscales. It has been shown that malnutrition predisposes poor perioperative outcomes in KOA patients. Preoperative optimization with close monitoring of metabolic markers and modifiable risk factors of malnutrition may help prevent acute periprosthetic fractures and associated infection and bleeding risks with fracture readmission (30).

Furthermore, malnutrition can increase the risk of surgical site infection in elective spine surgery and total joint arthroplasty. Therefore, preventing and controlling malnutrition plays an important role in orthopedic diseases. However, study results are inconclusive and often contradictory. Methodological differences for assessing nutritional status and KOA, diversity in study design and heterogeneity in study populations (healthy against sick) make it difficult to reach conclusions (31). Regarding the role of nutrition in KOA and the limitations of the studies carried out in this field, this study aimed to investigate the nutritional status and its association with the outcomes of KOA in these patients referred to the orthopedic clinics of educational centers, compared to non-suffered participants.

Materials and Methods

Study Design and Setting

This case-control study was based on data from the participants referred to the orthopedic clinics of the medical training centers affiliated with Ilam University of Medical Sciences, Ilam, Iran, April to June 2023. This study was carried out based on the guidelines of Declaration of Helsinki and approved by the Ethics Committee of Abadan University of Medical Sciences, Abadan, Iran (IR.ABADANUMS.REC.1401.131, 01/02/2023).

Study Participants and Sampling Method

The study population included outpatients of the two sexes aged 18 y or older, who were diagnosed with OA based on the 10th edition of the International Classification of Diseases. Moreover, patients with severe cardiovascular diseases (CVDs) such as heart failure (NYHA Class II-III), neurological diseases, severe mental diseases, pregnancy and lactating status as well as non-Iranian patients were excluded from the study (28). For practical reasons, patients with KOA diagnosed by an orthopedic specialist were categorized as KOA and referees without KOA, who were diagnosed by an orthopedic specialist and selected from the accompanying patients or other visitors to the clinic with no history of chronic and joint-destroying diseases, were categorized as non-KOA.

Sample Size

The sample size was calculated using the following formula and a similar study by Valentini et al. (16).

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$$\delta^2 = (\mu_1 - \mu_2)^2$$

$$n = \frac{(\sigma_1^2 + \sigma_2^2)(z_{1-\alpha/2} + z_{1-\beta})^2}{\delta^2}$$

A sample size of 50 participants per group provided 80% statistical power (power = 0.8) to detect a mean difference of 2.6 in the malnutrition score.

Demographic and Anthropometric Variables

Demographic variables, including age (y) and sex (male/female), were expressed in the categories. Age was classified into two groups of 1) age ≤ 40 y and age > 40 y, based on a similar study (24). Weight was assessed using digital scale (Seca, Japan) and height was assessed using portable stadiometer (Seca, Japan). The mathematical formula of weight (kg) to the square of height (m) was used to calculate the body mass index (BMI). The BMI classification was carried out as follows:

1- Underweight: < 18.5 kg/m^2

2- Normal weight: 9.24–5.18 kg/m^2

3- Overweight: 9.29–25 kg/m^2

4- Obese: ≥ 30 kg/m^2

Osteoarthritis and Knee Patellofemoral Outcome Questionnaire

The KOOS-PF is a specific knee-associated disorder questionnaire to assess patients' QOL (32). Nowadays, several questionnaires are available in original English to assess knee symptoms (33). In 2018, Crossley et al. (34) published and validated the KOOS-PF patella knee pain and osteoarthritis subscale. This subscale, which is completed by the patients, assesses pain score, stiffness and QOL in association with patellofemoral pain and osteoarthritis. The KOOS-PF is useful for assessing patients in clinical settings and investigating outcomes (35). Moreover, KOOS-PF is a subjective specific questionnaire that assesses knee discomfort caused by the patellofemoral joints and aims to estimate symptoms. Short and long-term performances in people with patellofemoral joint osteoarthritis have been developed as a subtype of knee osteoarthritis (36). The KOOS-PF includes 11 items that broadly assess symptoms caused by patellofemoral joints, including spasms, pain and QOL. The validity and reliability of KOOS-PF have been well-verified in patients with patellofemoral pain (24).

The KOOS has been translated into Persian and its validity and reliability have been verified in a previous study (34). In addition, cross-cultural validation of the KOOS-PF is carried out in multiple languages worldwide. A recent study with a systematic review design aimed at assessing the construct validity, reliability, responsiveness and interpretability of the patient-reported outcome assessments used to assess functions and pains in adults and adolescents with patellofemoral pain detected that KOOS-PF included the strongest assessment characteristics in patient-reported outcome assesses (37). In this study, KOOS-PF questionnaire was completed by a university student for each participant under the supervision of an orthopedic specialist and scores were assigned to each of the options based on the following scoring system of none = 0, little = 1, moderate = 2, severe = 3 and extremely severe = 4.

Dealing with Incomplete Answers

If a sign outside the designated houses for answering was reported, the closest one to the sign was considered as the answer. If two options were selected in response to two questions, the option that indicated the worst situation was selected as the answer. If more than two questions were unanswered, all the answers to that subscale were worthless and no score was assigned. It is noteworthy that no total score is available in the KOOS questionnaire; the scores of each subscale are calculated separately and the total score of each subscale is divided by the maximum possible score of that subscale. By tradition, in orthopedics, 100 is always suggested as no problem and 0 is suggested as the worst condition. To match this standard, scores of the subscales were normalized using the following formulas:

1- Spasm (cramping) (PF1): (100.4 × total score of the spasm subscale) - 100

2- Pain (PF2 to PF10): (36 / 100 × total pain subscale score) - 100

3- QOL (PF11): (100.4 × the overall score of the QOL subscale) - 100 (38, 39)

Mini-nutritional Assessment

Mini-nutritional assessment was designed and validated to provide a rapid unified assessment of the nutritional status of elderly patients in clinics, hospitals and nursing homes. The MNA consisted of simple assessments and short questions that could be completed in nearly 10 min (40). It contained questions about various issues linked to the elderly status, including cognitive impairment and depression, mobility, acute illness, mental stress, weight loss and food intake, which not only assessed malnutrition but also provided information on frailty and disability (41). Discriminant analysis was used to compare MNA findings with nutritional status assessed by physicians, using standardized comprehensive nutritional assessments, including full anthropometric parameters, clinical biochemistry and dietary parameters (40). In this questionnaire, points were specified to each option. The maximum total score was 30 and based on the points in the MNA questionnaire, people were categorized into three categories of 1) adequate nutrition (scores of 24–30), 2) at risk of malnutrition (scores of 17–23.5) and 3) protein-calorie malnourished (scores less than 17) (42). Based on the studies, this scale included 96% sensitivity, 98% specificity and 97% predictive. In general, the MNA scale is a predictor of mortality and hospital costs. Using

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this questionnaire, it is possible to identify people at risk of malnutrition (scores of 17–23.5) before drastic changing of weight or serum albumin. These people are more likely to decrease their caloric intake, which can be easily corrected with nutritional interventions (40). In this study, MNA questionnaire was completed by asking patients and by a trained university student under the supervision of a nutritionist.

Statistical Analysis

In this study, data analysis was carried out using SPSS software v.23 (IBM, USA). Kolmogorov-Smirnov test was used to check the normality of the data distribution. Then, data were analyzed using descriptive statistics, including mean, standard deviation (SD), frequency and percentage, to investigate basic characteristics of the participants. For the comparison of healthy groups with those with KOA, Mann-Whitney *U* test was used to analyze quantitative data with non-normal distribution, including age, malnutrition index score and the score of the subscales of spasm (cramping), pain and QOL. The KOOS-PF questionnaire and independent sample *t* test were used to analyze quantitative data with normal distribution, including BMI and body weight. In addition, Kruskal-Wallis H test was used to compare the outcome score of knee injury and arthritis between participants with various degrees of nutritional status in the two study groups. In addition, Chi-square test was used to analyze the classified data. Data were expressed as mean ±SD for quantitative variables and *n* (%) for categorical data. Then, bivariate parametric non-correlation test and Spearman's rho correlation coefficient were used to investigate the correlation between variables with non-normal distribution and results were expressed as *r* at a 95% confidence interval (CI). To investigate the relationship between nutritional status with and without KOA and the scores of pains, spasms and QOL subscales in participants, odds ratios (ORs) and 95% CI for the prevalence of protein-calorie malnutrition were calculated after adjustment for age, sex and BMI variables. Binary logistic regression analysis with Enter method was used to investigate the relationships. Before the analysis, participants were divided into three categories based on the nutritional status score of adequate, at risk of malnutrition and suffering from protein-calorie malnutrition. Degree of protein-calorie malnutrition was addressed as a reference. In a further analysis, participants were classified into two categories based on the pain, spasm and QOL subscale scores. Participants who were above the 50th percentile for the score of the subscales were reported with favorable statuses those with the subscale score lower than the 50th percentile were reported with unfavorable statuses. All statistical analyses were carried out using SPSS software v.23 (IBM, USA).

Results

Basic Demographic and Anthropometric Characteristics of the Participants

Results of comparing basic demographic and anthropometric characteristics between the two study groups are present in Table 1. As this table shows, a significant difference was seen between KOA and non-KOA groups for age. The mean age of patients with KOA was significantly higher than that of non-KOA participants. Moreover, 96% of KOA patients and 46% of non-KOA participants had ages greater than 40 y ($P \leq 0.001$). In addition, people who were overweight and obese showed a higher prevalence of KOA, compared to that underweight and normal-weight participants did ($P \leq 0.001$). However, the mean body weight was not significantly different between the two groups ($P = 0.072$). Prevalence of KOA in the two sexes did not show a significant difference ($P = 0.27$). This table shows that patients with KOA had a lower overall score of KOOS-PF and subscales of spasm, pain and QOL, compared to non-KOA participants. As stated in Materials and Methods, a score of 100 always includes no problem and 0 includes the worst condition in orthopedics, this result indicated more severe pains and spasms and lower QOLs in patients with KOA than in non-KOA participants.

Associations between Malnutrition and Knee Osteoarthritis

Comparison between the malnutrition index score and its degrees in KOA and non-KOA groups was carried out using Mann Whitney *U* test and Chi-squared tests, respectively (Table 2). Results indicated that KOA patients had a significantly lower mean score of malnutrition index ($P = 0.001$). In other words, these patients had a worse nutritional status than that non-KOA participants had. Prevalence of various degrees of malnutrition was significantly higher in patients with KOA than non-KOA prticipants ($P = 0.003$). Thus, 42 KOA patients (84%) were at risk of malnutrition and five patients (10%) were malnourished, while 34 participants without KOA (68%) were at risk of malnutrition and one participant (2%) suffered from malnutrition.

Figure 1 illustrates results of comparing KOOS-PF overall score means between the participants with various degrees of nutritional statuses (normal nutritional status, at risk of malnutrition and malnourished) in two groups with and without KOA. Results of Kruskal-Wallis H test showed no significant differences between the participants with various degrees of nutritional status for the overall score of the outcome of knee injury and arthritis ($P = 0.253$ and $P = 0.193$, respectively in KOA and non-KOA groups). Moreover, results of this test showed no significant differences between the participants with various degrees of nutritional statuses for the scores of the KOOS-PF subscales, including spasm, pain and QOL ($P < 0.05$).

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Table 1. Demographic, anthropometric and orthopedic characteristics of the study groups*

Group	Variable	KOA	Non-KOA	*P* Value
Age (y) □		±12.1 66.2	38.5±16.8	0.001≤
Age category□	40 ≤	(4) 2	54) (27	
	> 40	(96) (48	23 (46)	0.001≤
Sex□	Male	22 (55)	18 (45)	0.27
	Female	28 (46.7)	32 (53.3)	
Weight (kg)□		12.7 ± 74.4	68.6±18.9	0.072
BMI (kg/m^2)□	Normal	12 (24)	30 (60)	
	Overweight	26 (52)	9 (18)	≤0.001
	Obesity	12 (24)	(11 (22)	
KOOS-PF overall score□		17.1±23.9	98±4.6	0.001≤
Spasm subscale score□		20±29	99.5±3.5	0.001≤
Pain subscale score□		16.3±23	97.7±4.9	0.001≤
QOL subscale score□		22±33	98.5±6	0.001≤

*Data are expressed as Mean ± SD for quantitative and number (%) for categorical variables. ‡ The Mann Whitney *U* test was applied to analyze quantitative data with non-normal distribution.
□ The independent sample *t* test was used to analyze quantitative data with normal distribution.
□ The Chi-squared test was used to analyze categorical variables. Abbreviations: BMI, body mass index; QOL, **quality of life.**

Table 2. Comparison of malnutrition index and its degrees between the study groups

Group	Variable	KOA	Non-KOA	*P* Value
Malnutrition index score ‡		20.45±3.4	2±22.4	0.001
Degrees of malnutrition*				
Normal nutritional status		3 (6)	15 (30)	0.003
At risk of malnutrition		42 (84)	34 (68)	
Malnourished		5 (10)	1 (2)	

□ The Mann-Whitney *U* test analyzed quantitative data with non-normal distribution.
* The Chi-square test was used to analyze categorized data.

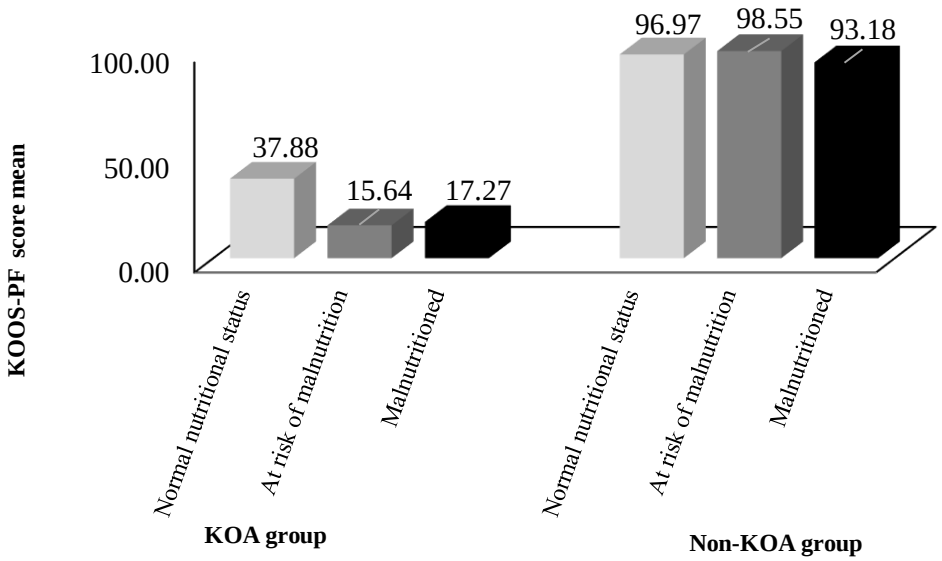


Figure 1. Comparison between the total scores of knee injury and arthritis outcome in participants with various degrees of nutritional status in the two study groups (P = 0.253 and P = 0.193 in KOA and non-KOA Groups, Respectively). Kruskal-Wallis H test was used

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Correlations of the Nutritional Statuses with Knee Osteoarthritis Subscales

Correlations between the malnutrition index score with the KOOS-PF overall score and the subscale scores of spasm, pain and QOL in the KOA group and non-KOA participants are present in Table 3. In patients with KOA, the QOL item score (PF-11) and the QOL subscale score increased significantly with the increase in the malnutrition index score (r = 0.297; CI, 0.045–0.549; P = 0.036). In patients with KOA, improved nutritional status was associated with better QOL in knee disorders caused by patellofemoral joints. However in participants without KOA, a significant negative correlation was observed between the malnutrition index score and score of the QOL subscale (r = -0.283; CI, -0.471 to -0.055; P = 0.049). In participants without KOA, a better nutritional status was associated with lower QOL. In participants without KOA, a significant positive association was detected between the malnutrition index score and score of the KOOS-PF2 item in the pain subscale. However, no significant correlation was observed between the malnutrition index score, KOOS-PF overall score and spasm and pain subscales score in the two study groups (P > 0.05).

Kruskal-Wallis H test was used to control the effect of BMI on the results of the correlation between the malnutrition index score and the KOOS-PF overall score as well as the scores of spasm, pain and QOL subscales. Results showed that in patients with KOA, the KOOS-PF overall score and its subscales did not show significant differences between the patients with various categories of BMI (underweight, normal weight, overweight and obese). Thus, BMI did not affect results of the associations between the malnutrition index score and KOOS-PF overall and subscales scores.

Assessing Risk of Knee Osteoarthritis and Subscales of Spasm, Pain and Poor QOL Based on the Nutritional Statuses

Bivariate logistic regression was used to investigate odds ratios at a 95% CI for KOA and subscales of spasm, pain and poor QOL based on nutritional statuses (Table 4). In unadjusted analysis, KOA, spasm, pain and QOL were associated with nutritional statuses. Participants with normal nutritional statuses were at a lower risk of having KOA, high spasm, increased pain and poor QOL, compared to malnourished participants with an OR of 0.04 (95% CI, 0.003–0.477; P = 0.011), 0.077 (95% CI, 0.007–0.833; P = 0.035), 0.057 (95% CI, 0.005–0.641; P = 0.02) and (95% CI, 0.007–0.833; P = 0.035), respectively. In bivariate logistic regression model, OR for the incidence of KOA and the subscales of spasm, pain and QOL compared between the normal nutritional, at risk of malnutrition and malnourished statuses after adjusting for age and sex included 0.033 (P = 0.03), 0.057 (P = 0.094), 0.052 (P = 0.052) and 0.057 (P = 0.094), respectively (Model 1). In addition, bivariate OR for the incidence of KOA and subscales of spasm, pain and QOL in normal nutritional status group included 0.024 (P = 0.019), 0.043 (P = 069), 0.045 (P = 0.043) and 0.043 (P = 0.069), respectively (Model 2), compared to the malnourished and at risk of malnourish groups after adjustment for age, sex and BMI. However, the association of spasm, pain and QOL with nutritional status after adjustment for study groups was not seen and only association of having KOA with nutritional status was seen in the model after adjustment for all variables, including age, sex, BMI and the study groups.

Table 3. Correlation coefficient (r) and 95% confidence interval (CI) between the score of the malnutrition index and subscales of spasm, pain and quality of life in the KOOS-PF questionnaire based on the study groups*

Variable / Group	KOA (n=50)		Non-KOA (n=50)	
	r (CI)	P Value	r (CI)	P Value
KOOS- PF1	-0.271 (-0.551 to -0.043)	0.057	0.195 (0.155-0.386)	0.175
KOOS-PF2	-0.213 (-0.477 to -0.061)	0.138	0.287 (0.048, 0.507)	0.044
KOOS-PF3	-0.269 (-0.493 to -0.0009)	0.059	0.096 (-0.118, 0.327)	0.505
KOOS-PF4	-0.222 (-0.475 to -0.036)	0.121	-0.06 (-0.174, 0.000)	0.679
KOOS-PF5	(-0.359 to -0.197) -0.091	0.53	0.145 (-0.256, 0.459)	0.316
KOOS-PF6	0.017 (-0.265 to -0.327)	0.906	0.224 (-0.033, 0.456)	0.118
KOOS-PF7	-0.110 (-0.394 to -0.224)	0.449	0.079 (-0.251, 0.326)	0.587
KOOS-PF8	0.015 (-0.29 to -0.331)	0.916	0.134 (0.209, 0.331)	0.355
KOOS-PF9	0.015 (-0.275 to -0.325)	0.918	0.088 (-0.275, 0.325)	0.548
KOOS- PF10	-0.236 (-0.513 to -0.025)	0.099	0.192 (-0.513, 0.025)	0.182
KOOS-PF11	0.297 (-0.549 to -0.045)	0.036	0.277 (-0.549, 0.045)	0.051
Overall score of KOOS-PF	0.263 (0.002, 0.524)	0.065	0.411, 0.165) (--0.153	0.294
Spasm subscale score	0.271 (-0.043, 0.551)	0.057	-0.196 (-0.386, -0.155)	0.177
Pain subscale score	0.245 (-0.023, 0.498)	0.086	-0.144 (-0.405, 0.17)	0.323
QOL subscale score	0.297 (0.045, 0.549)	0.036	-0.283 (-0.471, 0.055)	0.049

*Correlation test and Spearman's rho correlation coefficient were applied for data analysis. Abbreviations: KOA, knee Osteoarthritis; KOOS-PF1-11, knee injury and osteoarthritis outcome score or the score obtained from questions 1 to 11 in the KOOS-PF questionnaire; QOL, quality of life.

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Table 4. Associations of knee osteoarthritis with subscales based on KOOS-PF in subgroups with normal nutritional statuses (scores of 24–30), at risk of malnutrition (scores of 17–23.5) and malnourished (scores < 17) using mini-nutritional assessment questionnaire (two models of unadjusted univariate, one adjusting for age and sex and two adjusting for, age, sex and BMI)

	Unadjusted		Model 1		Model 2	
	Odds ratio (95% CI)	*P* Value	Odds Ratio (95% CI)	*P* Value	Odd ratio (95% CI)	*P* Value
Knee Osteoarthritis						
Normal nutritional status	0.04 (0.03, 0.477)	0.011	0.033 (0.02, 0.713)	0.03	0.024 (0.001, 0.549)	0.019
At risk of malnutrition	0.247 (0.028, 2.217)	0.212	0.174 (0.011, 2.869)	0.222	0.109 (0.07, 1.838)	0.124
Malnourished	Ref		Ref		Ref	
Spasm subscale						
Normal nutritional status	0.077 (0.007-0.833)	0.035	0.057 (0.002, 1.625)	0.094	0.043 (0.001, 1.272)	0.069
At risk of malnutrition	0.222 (0.025-1.933)	0.179	0.108 (0.005-2.555)	0.168	0.072 (0.003-1.764)	0.107
Malnourished	Ref		Ref		Ref	
Pain subscale						
Normal nutritional status	0.057 (0.005, 0.641)	0.02	0.052 (0.003, 1.022)	0.052	0.045 (0.002, 0.905)	0.043
At risk of malnutrition	0.234 (0.026, 0.102)	0.195	0.163 (0.01,2.548)	0.196	0.117 (0.007, 1.872)	0.129
Malnourished	Ref		Ref		Ref	
QOL subscale						
Normal nutritional status	0.077 (0.007, 0.833)	0.035	0.057 (0.002,1.625)	0.094	0.043 (0.001, 1.272)	0.069
At risk of malnutrition	0.222 (0.025,1.993)	0.179	0.108 (0.005,2.555)	0.168	0.072 (0.003,1.764)	0.107
Malnourished	Ref		Ref		Ref	

*The significance level was considered as $P<0.05$. *P* value was determined by bivariate logistic regression analysis. Model 1 is adjusted for age and sex and Model 2 is adjusted for age, sex and BMI.

Discussion

In this case-control study, possible associations between nutritional status and KOA were investigated using information of people referred to outpatient orthopedic clinics. Results of this study revealed that patients with KOA had a poor nutritional status, compared to that non-KOA people had. Prevalence of various degrees of malnutrition was significantly higher in patients with KOA than that without KOA. The findings showed that the normal nutritional status was associated with a lower risk of KOA after adjustment for age, sex and BMI, compared to malnourished nutritional status. Recently, role of nutrition in KOA has been assessed in various populations (43, 44). To the best of the authors' knowledge, this was the first study on associations between the nutritional statuses investigated using MNA and KOOS-PF questionnaire in adult patients.

Nutritional Status and Its Associations with Knee Osteoarthritis

Comparison between the study groups regarding nutritional statuses showed that a higher proportion of patients with KOA were at risk or suffering from malnutrition, compared to those of non-KOA participants. Moreover, results of bivariate regression analysis showed that participants with malnutrition had a 25-times higher risk of having KOA than that patients with a normal nutritional status had. The risk increased to 42 folds after adjustment for age, sex and BMI. This finding was similar to a recent study on Indian population reporting a high prevalence of malnutrition (69.5%) in patients with KOA based on albumin serum levels (45).

The current study has suggested a possible underlying mechanism to identify higher prevalence of malnutrition in patients with KOA, compared to that in non-KOA people. While the pathogenesis of OA is unclear, an experimental study on rats fed a low-protein diet has shown that this diet decreases systemic insulin-like growth factor-1 (IGF-I) (46). Since IGF-I is a major anabolic factor for cartilage homeostasis, dysregulation of protein malnutrition can affect cartilage and subchondral bone and may contribute to the development of osteoarthritis by altering the integrity of cartilage and subchondral bone (47). Another experimental study has detected that protein malnutrition lessens the bone anabolic effects of parathormone in female rats (48). As protein malnutrition is expected in older people (49), these mechanisms can be relevant to humans. Elderly patients often suffer from protein malnutrition, leading to a major alteration of the somatotropic axis and IGF-I production. Therefore, malnutrition can affect cartilage quality and contribute to the development of osteoarthritis. Identifying patients with malnutrition should be carried out early because the levels of key nutrients may take weeks to increase significantly (50). Patients with concerns for malnutrition should immediately be followed up with screening for food security, including geographic and resource-oriented ability to purchase healthy foods. Therefore, patient screening can be carried out by a nurse navigator or

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members of the care team and patients with identified undernutrition should be referred to a nutritionist or weight management specialist to design a highly individualized plan for the patients with differing levels of food security (51).

However, the current findings differed from those from the prevalence of malnutrition in the elderly people living in Iran, assessed using MNA questionnaire; in which, 28.1% of the participants suffered from inadequate nutrition. Variations in age, level of education, financial dependence, lifestyle (individual or social), health problems, multiple physical disabilities and chronic diseases, medication, smoking, and functional and cognitive statuses can explain differences in the results (52). Moreover, results of the present study showed a higher prevalence of KOA in overweight and obese people without significant effects on body weight, compared to underweight and normal-weight people. Because patellofemoral pain is part of a degenerative joint disorder in middle-aged and older populations with patellofemoral osteoarthritis (35), such results were not unexpected. Similar to these results, Studies on South Korean (53) and Iranian (52) populations reported higher risks of OA and increased pains with higher BMI and poor health statuses in older populations. One hypothesis that possibly explains the association between obesity and OA includes the metabolic theory (54, 55). Pro-inflammatory factors such as C-reactive protein, interleukin-6 and plasminogen activator inhibitor type 1 are majorly released by abdominal and visceral adipose tissues, which may negatively affect joint structures and accelerate development of OA (56). The second theory widely accepted in the literature includes biomechanical theory (57, 58). This theory states that the protrusion of the abdomen by shifting the body's center of gravity leads to hip introversion, knee valgus and flat feet, which are associated with excesses in weight and changes in walking, leading to joint stresses.

Nutritional Status and Its Association with the Spasm Subscale in Knee Osteoarthritis

Correlation analysis showed no significant associations between the study groups' spasm subscale scores and malnutrition index scores. In the unadjusted regression analysis, high spasm was significantly associated to nutritional statuses. Individuals with adequate nutritional status were at a lower risk of developing spasm than that individuals with malnutrition were. However, this association was not reported after adjusting for sex, age, BMI and study groups. Thus, nutritional status possibly did not affect spasm status in KOA.

Nutritional Status and Its Association with Pain Subscale in Knee Osteoarthritis

In people without KOA, significant positive correlations were reported between the malnutrition index score and the score of the KOOS-PF2 item in the pain subscale. In unadjusted regression analysis, suffering from high pain was significantly correlated to nutritional statuses. Therefore, people with adequate nutritional statuses were at a lower risk of suffering from high pain, compared to that people with malnutrition were. This risk increased to 22-fold after adjustment for age, sex and BMI. This finding was similar to that of a community-based cross-sectional study on Korean women over 50 years old, 2021; in which, knee pain independent of arthritis was associated to poor diet quality in these women (59). However, the association between pain incidence and nutritional status was not reported after adjusting for study groups, age, sex and BMI, similar to a study on KOA to clarify the mediating role of BMI in affecting associations between age, knee circumference and pain (60). Regarding contradictions in results of the present study and those of previous studies, needs of further studies with greater sample sizes and controlling the possible condetecteders seem critical to find exact relationships between nutritional status and pain in KOA.

Nutritional Status and Its Association with QOL subscale in Knee Osteoarthritis

In patients with KOA, subscale score of the QOL increased significantly with increases in score of the malnutrition index. In other words, a better nutritional status was associated to a higher QOL in patients with knee problems caused by patellofemoral joints. However, in people without KOA, a better nutritional status was associated to a lower QOL, similar to a study by Abdelaleem and Rizk in Egypt on patients with bilateral medial tibiofemoral knee osteoarthritis; in which, all patients completed the KOOS questionnaire. This study showed that KOOS was a good indicator of physical function in patients with KOA and provides information on the effect of knee-linked disability on QOL (32).

Limitation of the present study included that serologic markers of malnutrition in participants were not assessed due to the limited finance. Results of this study help manage KOA patients through orthopedic specialists and physiotherapists, who carry out physical examinations. These findings enable them to have a broader understanding of KOA. This study was carried out to understand the nutritional predictors of KOA and roles of nutritional status in osteoarthritis and knee-patellofemoral outcomes. Regarding higher prevalence of malnutrition in patients with KOA and correlations between the nutritional statuses of patients with KOA and the consequences of this disease including QOL, it is suggested that studies further investigate various dietary patterns associated to the progression of KOA and its symptoms. To the best of the authors' knowledge,

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Western and cautious nutritional patterns have been investigated in recent studies regarding development of KOA (9, 61). Further studies can benefit from prospective longitudinal studies to assess relationships between malnutrition degrees and KOA and how each degree leads to KOA. In addition, clinical trials are suggested to investigate effects of interventions for the improvement of nutritional status on the outcomes of KOA, including knee pain, joint stiffness and physical dysfunction.

Conclusion

in conclusion, prevalence of malnutrition was 10% in KOA outpatients and MNA was used to detect malnutrition in these patients. The current study recommends routine assessment of the nutritional status of all KOA patients to correct the nutritional abnormality, resulting in a better QOL linked to the consequences of KOA and its decreased complications. Results represent an important milestone in clinical rehabilitation, especially for orthopedic specialists and physical therapists, enabling them to develop and design interventions to improve the nutritional status of KOA patients.

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Authors' Contributions

Naghashpour M, conceptualization, methodology, software, writing—original draft, funding acquisition; Karimiyarandi H, visualization, investigation, Varmaghani A, data curation; Mohammadi SM, supervision, validation; Golabi S, writing—reviewing and editing.

Ethical Considerations

Before starting the study, participants were informed on the study's purposes and procedures. In addition, participation in the study did not cause financial burdens for the participants and private and personal information of the volunteers were protected. Moreover, study results were explained to the volunteers.

Disclosure Statement

No potential conflicts of interest were reported by the authors.

Abbreviations

KOA, knee osteoarthritis
OA, osteoarthritis
QOL, quality of life
KOOS-PF, knee injury and osteoarthritis outcome score-patellofemoral
MNA, mini-nutritional assessment
BMI, body mass index
ORs, odds ratios
Cis, confidence intervals

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