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The effects of risk factors on knee osteoarthritis outcomes in elderly patients in Iran

Afsaneh Bakhtiari [1], Mahbobeh Pourali [2], Khodabakhsh Javanshir [3] ✉ *

1. Mobility Impairment Research Center, School of Public Health, Babol university of Medical Sciences, Babol, Iran.
2. Department of Nursing, School of Nursing and Midwifery, Babol University of Medical Sciences, Babol, Iran.
3. Mobility Impairment Research Center, School of rehabilitation, Babol University of Medical Sciences, Babol, Iran.

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ABSTRACT

Background: Knee osteoarthritis (KOA) is the most common joint disease in the elderly and one of the main causes of disability. Although many studies have been conducted on the osteoarthritis risk factors, studies on the outcomes of risk factors of KOA are limited. Therefore, this study aimed at exploring the outcomes of contributing risk factors in older adults with KOA.

Methods: The study was conducted on 332 older adults with KOA. Knee injury and Osteoarthritis Outcome Score (KOOS) was applied to measure KOA outcomes and outcomes risk factors questionnaire were completed to assess potential explanatory variables. Univariate analysis and multivariate logistic regression were done to identify the risk factors for KOA outcomes.

Results: The results of multiple linear regression analysis showed that repetitive use of joints (B= -0.420 to -0.509, p <0.001) and diabetes (B=-0.250, p <0.01 to -0.445, p <0.001) were the most common risk factors related to all KOA outcomes, followed by BMI (B=-0.247, p<0.05 to -0.458, p<0.001) and multimorbidity (B =-0.225, p<0.01 to -0.345, p<0.001). Increasing age, gender, and hypertension variables were associated with only some of the KOA outcomes, which generally included a decrease in sport/recreation, quality of life, activity daily living and an increase in pain and other symptoms.

Conclusion: The multiplicity of chronic diseases can complicate the KOA outcomes by influencing management decisions. Although, proper management of chronic diseases can improve the KOA outcomes, more studies on multimorbidity in KOA are needed. Pay attention to the guidelines for preventing the KOA outcomes by focusing on lifestyle modification, correct use of the knee joint and weight control, is necessary in future researches.

Keywords: Knee osteoarthritis, Outcomes, Risk factors, Iran, Elderly.

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* **Corresponding Author:** Khodabakhsh Javanshir
Address: Mobility Impairment Research Center, School of rehabilitation, Babol University of Medical Sciences, Babol, Iran.
Tel: +989111140315 **E-mail:** kjavanshir@yahoo.com

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Introduction

Osteoarthritis (OA) is the most common disorder that disrupts the mobility of people especially older adults (1). The knee joint is the most common site affected by OA. Nearly half of people aged 50 years or more, experience knee pain during their lifetime and a quarter suffer from severe and uncomfortable knee pain (2, 3). Therein percent of women and 11% of men over the age of 60 years show signs of KOA (4), that in many cases leads to joint surgery (5, 6). The other OA outcomes include stiffness and discomfort of the knee joint, which can interfere with daily life, work activities, mobility, exercise, and recreational activities (7, 8).

Movement disorders restrict the elderly to a sedentary lifestyle, which not only expose them to increased health risks but also increase their dependency. These conditions cause psychological effects, which leads the elderly to isolation (9). Complications of OA can affect QOL in the older adults (10, 11). There are currently no definite and reliable treatment methods available for these difficulties (12, 13). Hence, focusing on risk factors and improving preventable or corrective conditions can be very important and valuable for this population.

A number of the possible risk factors for KOA have been discussed in literature namely weight gain, being female, the age over 60 years, familial history, smoking (9), obesity (14, 15), low level of education (16), mobility status (5), quadriceps muscle weakness (17), vitamin D deficiency (18), and systemic diseases such as Gout, Rheumatoid Arthritis, and Hemophilia (19). Also, biomechanical factors consist of trauma, a history of serious knee injury (20), knee injury during exercise, and recreation have been considered as possible risk factors in this condition (5). Besides, psychological factors namely depression and occupation related factors seem influential (21) in developing or exacerbating KOA.

To the best of our knowledge, there is no comprehensive study that examines the risk factors of KOA outcomes in Iranian elderly; in accordance with the results of recent systematic review study (10), which showed that few studies have been conducted in Asian countries in general and developing ones in specific on the possible outcomes of KOA risk factors. Moreover, the health-related conditions in this population impose a considerable cost with regard to economic issues on the government. Therefore, figuring out and managing possible risk factors using the development of preventive strategies would be so critical and indispensable in various dimensions of life in senior citizens. Hence, the goal of the present study is to investigate the risk factors of the KOA outcomes in older adults in Iran.

Methods

Design and Study population

The participants were 336 older adults aged 60 years and over, living in Babol city, Mazandaran province, Iran. Participants included elderly of both genders who referred to the physical therapy department of Yahyanejad Hospital affiliated with Babol University of Medical Sciences, with prior diagnosis of KOA by an orthopedist or rheumatologist. Eligible participants were those who complained of unilateral or bilateral knee pain and referred for physiotherapy. The samples were all independent and ambulate, with no assistive devices and no history of knee surgery, significant hip or spinal arthritis, and a recent serious illness.

All samples met American College of Rheumatology (ACR) clinical classification criteria for KOA (16). The ACR clinical classification criterion for KOA is a popular method of classifying KOA. In these criteria the presence of knee pain along with at least three of the following six items can classify the KOA in the patients: age> 50 years old, morning stiffness < 30 minutes, crepitus on knee motion, bony tenderness, bony enlargement, no palpable warmth. The patients were examined by an experienced physiotherapist who worked with such patients for more than 20 years to confirm that the

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samples have met the ACR criteria. The patients were excluded from the study for the absence of consent or incompletely filled out questionnaire. Finally, 332 questionnaires out of the total of 336 were analyzed. The questionnaires were completed by participants in the presence of the researcher; for illiterate individuals, the researcher completed the questionnaire on their behalf.

Measurements and tools

Weight was measured by SECA Digital Scale, which was calibrated with 1 kg of known weight and with the accuracy of 100 gm. Height was determined by a stadiometer in standard conditions. Body Mass Index (BMI) was calculated as weight (in kg) divided by height in meters squared. KOA outcomes risk factors questionnaire were completed to assess potential explanatory variables. KOOS was also applied to measure KOA outcomes.

Risk factors

KOA risk factors were divided into four categories including: unmodifiable risk factors (age, gender, KOA family history), pathophysiological conditions (diabetes, hypertension, cardiovascular disease, multimorbidity, polypharmacy), lifestyle factors (BMI ≥25, smoking, repetitive use of joints at work, exercise, Vitamin D intake, history of self-reported hip injury) and socio-economic factors (area of residence, marital status, educational level, income adequacy).

Outcomes of KOA

KOOS questionnaire covers both the short-term and long-term outcomes of KOA. The KOOS is a 42-item disease-specific questionnaire with five subscales: Pain (nine items); Symptoms (seven items); ADL (17 items); Sport and Recreation, (five items), and QOL (four items). A five-point Likert scale ranging from Zero (no problems) to four (extreme problems) is used for scoring each item and each of the five scores is calculated as the sum of the items included. Raw scores are transformed to a 0-100 scale with Zero indicating extreme problems and 100 indicating no problems. Scores between 0 and 100 represent the percentage of total possible score achieved. The total score is not calculated because it is desirable to analyze and interpret the five subscales separately. This questionnaire was validated for Iranian population by Salavati M, et al. The results showed that Persian-version of the KOOS is a culturally-adapted, reliable and valid outcome measure to be used in Iranian patients (17). The normalization of KOOS subscale scores is shown in table 1.

Ethics approval

All procedures were carried out on the basis of ethics standards of the responsible committee on human experimentation (institutional and national) and to the Declaration of Helsinki. In addition, the ethics Committee of Babol University of Medical Sciences approved the study (NO.:MUBABOL.REC. 1394.350). All participants provided an informed written and signed consent form.

Statistical analysis

SPSS version 23 software (SPSS Inc., Chicago, IL) was used to analyze the data. Continuous variables were represented by using mean and standard deviation (SD). Normality of distribution was ascertained by the Kolmogorov–Smirnov test. We used independent sample t-test to assess bivariate associations between class explanatory variables (socio-demographic indicators and KOA risk factors) and five subscales of KOOS questionnaire. Multiple linear regression analysis was performed to identify independent variables associated with subscales of KOOS questionnaire. For the all models, the presence of knee pain, symptoms, ADL limitations, Sport/Rec limitation and reduced knee-related QOL were selected as the dependent outcome variables. Collinearity between the independent variables in all models using the Tolerance and Variance inflation factor test showed that the tolerance rate for all variables was from 0.859 to 0.997. Also, the inflation rate of variance was 1.164-1.003 which indicates a low level of collinearity. Variables significantly (p <0.05) associated with knee

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problems from bivariate analyses were entered simultaneously into inter and then backward stepwise model for each subscale. Also, the R square was reported to determine the percentage of the variance of the dependent variable described by the independent variables in each subclass. Standardized coefficient β with 95% confidence intervals were calculated.

Table 1. The normalization of KOOS subscales scores

KOOS subscales	Normalization of KOOS sub-scales scores
Pain	$\frac{\text{pain subscale total score X 100}}{36}$
Symptoms	$\frac{\text{symptoms subscale total score X 100}}{28}$
ADL	$\frac{\text{ADL subscale total score X 100}}{68}$
Sport/Rec	$\frac{\text{Sport/Rec subscale total score x 100}}{20}$
QOL	$\frac{\text{QOL subscale total score X 100}}{16}$

Results

The average age of the participants was 68.35 ± 5.49 with a BMI of 28.36 ± 3.89. Most of the problems of the KOOS subscales belonged to Sport /rec function with an average of 10.23 ± 6.46 and then to QOL (27.50 ± 9.48), Pain (47.32 ± 14.05), ADL (51.18 ± 15.04) and the other symptoms (52.03 ± 9.74) respectively. The demographic characteristics of the participants and the risk factors of KOA are shown in table 2. Bivariate analyses (table 3) showed that people over the age of 74 had a significant problem with all subscales of the KOOS, except for other symptoms, which were similar to those under 74 years of age. This means that both groups complained of dryness and discomfort in the knee on average. Women reported significantly more problems on all KOOS subscales, although were similar to men in pain intensity and QOL. Knee-related QOL values were low in both genders, but in women it was much lower than in men. Familial history of KOA had no effect on the OA outcomes.

Among the pathophysiological factors, diabetes and hypertension showed a significant relationship with all KOOS subscales. Also, multimorbidity was significantly associated with decreased ADL and QOL and increased pain. Elderly with polypharmacy had significantly more symptoms and pain and less Sport/Rec. Obesity and weight gain from lifestyle factors, showed a significant relationship with all subscales of the KOOS, except for ADL and QOL. Similarly, the history of knee injury was significantly associated with all KOOS subscales other than ADL and Sport/Rec. Repetitive use of joints at work also showed a significant relationship with all the subscales of KOOS. Among the socioeconomic factors, marital status was significantly associated with all KOOS subscales, meaning that single people experienced significantly more problems with KOA. Income adequacy, education and area of residence did not show any significant relationship with the KOA outcomes (table 3).

Table 4 shows the results of multiple linear regressions of KOA risk factors for KOOS subscales. The largest B coefficient for KOA symptoms was related to the repetitive use of joints (B = -0.509, p <0.001), followed by gender (B = 0.330, p <0.001). This means that the significant effect of gender on the knee symptoms increased from men to women. Diabetes (p <0.012), overweight / obesity (p <0.028), and hypertension (p <0.023) also showed a significant association with knee symptoms. The repetitive use of joints was the strongest predictor of knee pain (B= -0.480, p <0.001). Subsequent significant variables were obesity with B= -0.414, followed by diabetes (B= -0.321), and multimorbidity (B = -0.225), respectively. ADL limitation increased with the repetitive use of joints (B = -0.532, p <0.001), diabetes (B = -0.445, p <0.001), and multimorbidity (B = -0.284, p <0.021).

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Having the age over 74 years old, had the highest B coefficient in Sport / Rec limitation (B = -0.520, p <0.002), followed by overweight/obesity (B = -0.458, p <0.001), and repeated use of Joint (B = -0.420, p <0.001). The largest coefficient of determination was related to this model, as the model showed that 43% of the changes in the Sport / Rec function were affected by the relevant independent variables. Knee related QOL decreased with repeated use of the joint (B = -0.494, p <0.001), diabetes (B = -0.363, p <0.022), multimorbidity (B = -0.345, p <0.001), and increase age over 74 years (B = -0.263, p <0.003).

Table 2. The characteristics of participants and osteoarthritis knee risk factors

Demographic variables	N (%)	KOA risk factors variables	N (%)
Age group		**KOA family history**	
60-74	288 (86.7)	Yes	260 (78.3)
≥ 75	44 (13.3)	No	72 (21.7)
Gender		**BMI**	
Women	213 (64.2)	≤24.9	59 (17.8)
Men	119 (35.8)	25-29.9	155 (46.7)
Marital Status		≥30	118 (35.5)
Married	270 (81.3)	**Self-reported prior hip injury [1]**	
Widow/divorced/single	62 (18.7)	Yes	56 (16.9)
Residence		No	276 (83.1)
Urban	181 (54.5)	**Repetitive use of joints at work [2]**	
Rural	151 (45.5)	Yes	130 (39.2)
Education		No	202 (60.8)
Illiterate	168 (50.6)	**Currently smoking**	
Primary/middle school	115 (34.6)	Yes	45 (13.9)
High school	38 (11.5)	No	286 (86.1)
University	11 (3.3)	**Exercise (≥30 min/d)**	
Financial dependency		Yes	42 (12.7)
Dependent	62 (18.7)	No	290 (87.3)
Independent	270 (81.3)	**Multimorbidity [3]**	
Family Income		Yes	73 (21.99)
Inadequate	193 (58.2)	No	259 (78.01)
Almost enough	116 (34.9)	**Polypharmacy [4]**	
Adequate	23 (6.9)	Yes	95 (28.6)
Live with		No	237 (71.4)
Alone	44 (13.3)	**Vitamin D intake**	
Spouse	250 (75.3)	Yes	58 (17.5)
Children	38 (11.4)	No	273 (82.5)

1. Knee injuries mean injuries to several structures, including ligaments, meniscus, cartilage, etc.
2. Repetitive use of joints at work was based on self-reports of frequencies of four employment-related activities: squatting, standing, lifting and walking (0=never, 1=seldom, 2=sometimes, 3=often, 4=always). The sum (0–16) of the individual scores was dichotomized as no (<10) or yes (≥10).
3. Multimorbidity was defined as the simultaneous presence ≥three chronic diseases.
4. Polypharmacy was defined as daily consumption >4 prescribed drugs.

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Table 3. Association between osteoarthritis knee risk factors and KOOS subscales; Bivariate

Variables	Symptoms	Pain	ADL	Sport/Rec	QOL
Unmodifiable risk factors					
Age					
<74 year	49.95±11.05	46.14±13.78[1]	49.91±14.98[1]	7.04±3.63[1]	27.61±8.91[2]
≥74 years	48.39±10.75	36.18±12.82	41.35±13.56	2.72±0.23	24.33±10.21
Gender					
Men	52.44±11.18[1]	46.63±15.39	51.24±16.57[2]	9.87±2.72[2]	30.41±9.76
Women	48.24±10.64	43.82±13.18	47.39±14.00	4.59±1.80	25.77±8.79
Family history of KOA					
Yes	49.25±10.88	44.50±14.10	48.79±15.24	6.01±1.22	27.07±9.63
No	51.50±11.21	46.66±13.70	49.36±13.83	8.56±1.18	29.31±8.17
Pathophysiological factors					
Diabetes					
Yes	44.88±12.60[1]	40.44±14.78[1]	44.36±15.93[1]	4.20±0.56[2]	25.41±9.20[2]
No	51.21±10.05	46.15±13.58	50.11±14.56	7.13±1.38	28.04±9.39
Hypertension					
Yes	54.87±11.39[1]	41.02±14.47[1]	45.79±16.27[2]	4.31±0.42[3]	27.63±8.72
No	51.32±10.46	46.37±13.61	49.99±14.40	7.33±1.87	27.36±9.68
Cardiovascular disease					
Yes	48.04±11.86	42.59±15.41	48.83±16.63	3.67±0.62[1]	26.83±9.99
No	50.37±10.63	45.64±13.46	48.75±14.48	7.46±1.59	27.66±9.19
Multimorbidity					
Yes	50.26±10.78	35.16±12.52[1]	43.52±10.63[1]	4.55±0.65	21.63±9.28[1]
No	52.45±11.32	45.24±11.88	50.25±12.46	6.37±1.10	30.45±9.58
Polypharmacy					
Yes	40.56±13.98[1]	37.21±15.37[1]	45.24±15.75	2.50±0.62[1]	25.98±8.63
No	50.98±10.09	45.24±13.73	48.83±15.11	6.53±1.47	27.88±9.45
Lifestyle factors					
BMI					
≤24.9	52.65±10.07[2]	47.19±16.02[1]	50.26±15.61	9.32±2.31[3]	29.49±8.07
≥25	48.99±11.17	38.08±13.64	48.24±14.92	5.71±1.90	26.92±9.30
Smoking					
Yes	49.13±10.70[2]	44.43±13.98	48.27±14.97	6.26±1.22	27.29±9.26
No	53.61±12.32	47,73±14.17	51.92±15.56	7.90±1.36	28.16±10.26
Repetitive use of joints at work					
Yes	42.68±10.50[1]	40.58±14.62[1]	43.28±14.33[1]	3.22±0.50[1]	21.47±9.29[1]
No	53.32±11.12	46.24±12.38	52.21±15.47	9.17±1.45	30.10±9.28

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Variables	Symptoms	Pain	ADL	Sport/Rec	QOL
Exercise					
Yes	54.32±9.65	50.32±12.66	55.81±14.45	10.13±2.76	28.54±7.71
No	50,00±8.45	47.22±10.67	42.66±12.35	6.21±1.32	18.75±4.35
Vitamin D intake					
Yes	52.18±10.26	47.43±11.60	50.26±13.63	8.46±1.12	29.20±8.34
No	49.78±10.58	45.56±12.11	48.98±14.20	6.69±1.30	27.31±9.18
History of Self-reported hip injury					
Yes	45.99±11.21[3]	40.77±12.75[2]	45.73±15.31	4.77±0.85	21.40±9.44[3]
No	50.39±10.99	45.35±14.12	49.18±14.83	6.57±1.08	28.22±9.84
Socioeconomic Status					
Education level					
<12 years	49.81±11.06	44.65±14.12	48.67±15.04	6.44±1.28	27.53±9.43
≥ 12 years	47.79±9.32	49.83±11.44	51.80±16.05	7.00±0.96	24.37±8.04
Area of residence					
Rural	49.50±10.25	44.19±13.73	47.94±14.70	5.73±1.67	24.83±9.35[1]
Urban	50.04±11.87	45.59±14.44	49.77±15.46	7.33±1.78	30.55±8.49
Marital status					
Married	50.46±11.09[3]	45.57±14.36[2]	49.71±15.33[3]	7.29±2.72[1]	28.38±9.13[1]
Single	46,65±10.12	41.56±12.22	44.70±13.19	2.90±0.56	23.36±9.55
Income					
Adequate	52.01±11.72	40.16±13.92	46.41±16.10	11.08±3.69	30.10±9.89
Inadequate	51.68±10.76	46.13±14.68	49.17±15.13	10.34±2.`8	28.26±10.18

1. $p<0.001$ 2. $p<0.05$ 3. $p<0.01$.

Table 4. The regression coefficient of osteoarthritis knee risk factors on KOOS subscales in elderly people

KOOS subscale	Variable	B (CI)	p
Other symptoms			
R2=0.032	**Gender** (men vs. women)	0.330 (0.263 to 0.771)	0.001
	Diabetes (yes vs. No)	-0.250 (-0.301 to -0.131)	0.012
	Hypertension (yes vs. No)	-0.073 (-0.086 to -0.061)	0.023
	Polypharmacy (yes vs. no)	-0.274 (-0.723 to 0.39)	0.286
	BMI (≥25vs. ≤24.9)	-0.247 (-0.304 to -0.130)	0.028
	Currently smoking (yes vs. No)	-0.143 (-0.412 to 0.113)	0.310
	Repetitive use of joints (yes vs. No)	-0.509 (-0.784 to -0.232)	0.001
	Self-reported prior hip injury (Yes vs. No)	-0.021 (-0.029 to 0.019)	0.451
	Marital status (Married vs. single)	0.108 (-0.062 to 0.328)	0.223

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KOOS subscale	Variable	B (CI)	p
Pain			
R2=0.038	**Age** (≥74 vs. <74 year)	-0.408 (-0.293 to 0.786)	0.368
	Diabetes (yes vs. no)	-0.321(-0.410 to -0.033)	0.028
	Hypertension (yes vs. no)	-0.128 (-0.175 to 0.098)	0. 562
	Multimorbidity (yes vs. no)	-0.225 (-0.310 to -0.134)	0.011
	Polypharmacy (yes vs. no)	-0.151 (-0.326 to 0.176)	0.379
	BMI (≥25vs. ≤24.9)	-0.414 (-0.527 to -0.346)	0.001
	Repetitive use of joints (yes vs. no)	-0.480 (-0.604 to -0.285)	0.001
	Self-reported prior hip injury (Yes vs. no)	-0.025 (-0.040 to 0.128)	0.584
	Marital status (Married vs. single)	0.134 (-0.031 to 0.025)	0.384
ADL			
R2=0.031	**Age** (≥74 vs. <74 year)	-0.376 (-0.298 to 0.747)	0.652
	Gender (men vs. women)	0.238 (-0.408 to 0.685)	0.471
	Diabetes (yes vs. no)	-0.445 (-0.512 to -0.225)	0.001
	Hypertension (yes vs. no)	-0.103 (-0.158 to 0.194)	0.320
	Multimorbidity (yes vs. no)	-0.284 (-0.310 to -0.157)	0.021
	Repetitive use of joints (yes vs. no)	-0.532 (-0.607 to -0.222)	0.001
	Marital status (Married vs. single)	0.126 (-0.062 to 0.392)	0.287
Sport and recreation function			
R2=0.043	**Age** (≥74 vs. <74 year)	-0.520 (-0.697 to -0.308)	0.002
	Gender (men vs. women)	0.287 (3.931 to 8.427)	0.022
	Diabetes (yes vs. no)	-0.345 (-0.450 to -0.094)	0.001
	Hypertension (yes vs. no)	-0.011 (-0.036 to 0.001)	0.385
	CVD (yes vs.no)	-0.133 (-0.221 to 0.096)	0.448
	Polypharmacy (yes vs. no)	-0.026 (-0.047 to 0.056)	0.715
	BMI (≥25vs. ≤24.9)	-0.458 (-0.582 to -0.319)	0.001
	Repetitive use of joints (yes vs. no)	-0.420 (-0.629 to -0.346)	0.001
	Marital status (Married vs. single)	0.164 (-0.054 to 0.212)	0.428

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KOOS subscale	Variable	B (CI)	p
QOL			
R2=0.040	**Age** (≥74 vs. <74 year)	-0.263 (-0.464 to -0.098)	0.003
	Diabetes (yes vs. no)	-0.363 (-0.450 to -0.094)	0.022
	Multimorbidity (yes vs. no)	-0.345 (-0.521 to -0.168)	0.001
	Repetitive use of joints (yes vs. no)	-0.494 (-0.592 to -0.266)	0.001
	Self-reported prior hip injury (Yes vs. no)	-0.028 (-0.040 to 0.126)	0.392
	Area residence (urban vs. rural)	0.292 (-0.542 to 0.452)	0.126
	Marital status (Married vs. single)	0.193(-0.084 to 0.354)	0.265

Discussion

The current study aimed at determining the possible risk factors of KOA outcomes among the Iranian elderly. The results showed that repetitive use of joints and diabetes were the most related risk factors in the KOA outcomes, followed by weight gain, obesity, and multimorbidity respectively. Increasing age, gender, and hypertension were associated with only some of the KOA outcomes, which generally included a decrease in Sport/Rec, QOL, ADL and an increase in pain and other symptoms. However, other factors did not show significant associations in multiple linear analysis plenty of studies have been conducted on the risk factors for osteoarthritis, surveys on the risk factors of KOA outcomes in the elderly are limited. As far as we know, the current research is the first study in this field in Iran.

The results demonstrated that repetitive use of joints had the most significant positive correlation with all KOOS subscales in elderly subjects. Our findings are consistent with the findings of some other researchers who reported that repetitive use of joints at work may predispose the involved joint to OA (18). Some regional studies showed that frequent joint use is a common risk factor in Asian people for the risk of OA (10, 19). According to Research on Osteoarthritis- Osteoporosis against Disability (ROAD) in Japan, occupations that involve squatting or kneeling for more than two hours a day are associated with a higher risk of moderate to severe KOA. In addition, the study also showed that Japanese people over the age of 60 who climb more than 1 hour a day, standing more than 2 hours a day and carry loads weighing 10 kg or more at least once a week and walking more than 3 kilometers a day were associated with an increased risk of radiographic KOA (20).

Formerly, the OA development was ascribed to the aging process due to progressive degeneration. However, many researchers deem that the true process is a microtrauma accumulation, the rate of which clearly rises with age. Therefore, OA that emerges in the elderly results from the accumulation of microtrauma. That is why some people who are more exposed to certain microtraumas develop OA so early. Microtraumas that are easily encountered in the workplace include vibrations and mechanical shocks transmitted by machines and certain objects, as well as disorders caused by specific movements and work positions (18, 21).

Present findings showed that diabetes also had a significant positive correlation with all KOOS subscales. Some studies reported association between diabetes and OA (22-24). Veronese et al. (2019) showed that patients with diabetes had 2.1 times odds of developing KOA compared to patients who did not have diabetes (25). Recent studies of metabolic syndrome-associated OA have concentrated on a better understanding of the role of metabolic diseases in inducing or worsening joint damage. Studies

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have reported an association between OA and several components of the metabolic syndrome, such as hypertension and type 2 diabetes, independent of obesity or other known risk factors for osteoarthritis. (26, 27). The results of various studies show the deleterious effect of abnormal lipid and glucose on homeostasis of articular cartilage (28, 29). Chronic low-grade inflammation is present in OA and metabolic disorders and may have a role in genesis of both (27). Thus, OA is emerging as a disease that has different forms including a metabolic form, in addition to the age-related and injury-related forms.

Considering that diabetes and OA are metabolic disorder, the detrimental effect of hyperglycemic conditions might alter the normal process of metabolism of articular cartilage and prearthicular tissues (30). This can be exacerbated by aging, which is associated with a higher prevalence of diabetes. The results of a 20-year longitudinal cohort study on 927 patients showed that T2DM could predict both joint failure and knee and hip arthroplasty independent from gender, age, and BMI (31). Health of articular cartilage depends on metabolic factors that support cartilage's growth and nutrition, and altering them can lead to impairment. There are a number of studies showing a direct link between altered glucose metabolism and OA (22-24, 30). However, more studies are needed to understand whether controlling and preventing diabetes can affect the outcomes of osteoarthritis. Furthermore, obesity-related OA can affect not only weight-bearing joints but also other joints, including the hands, suggesting the contribution of circulating mediators released by adipose tissue known as adipokines (32). Therefore, OA may have a systemic metabolic component. Evidence from epidemiological and biological studies supports the idea of metabolic OA, defined as a broad clinical phenotype that includes obesity-related OA (29).

Our results showed a significant positive correlation between BMI and three subscales of KOOS including pain, sport and recreation function and other symptoms. Pooled Risk Ratio showed that being overweight or obese predisposes knee to have OA approximately 2.5 and 4.6 times more than having normal weight. Five kg/m2 increase in BMI tends to 35% increase of the risk of knee OA (32). Our findings are consistent with results of previous studies (15, 33). Based on Manninen et al, weight gain in adulthood can slightly increase the risk of OA leading to knee replacement compared to keeping the weight constant (34). Therefore, it is very important to consider weight control of elderly in health policies as an important issue.

In present study, multimorbidity was a strong predictor of KOA, after repetitive joint use and diabetes. The first systematic review on the KOA (2019) has found that people with OA are more likely to have other chronic conditions, especially stroke, peptic ulcer, hypertension and depression (35). Whether these comorbidities just co-exist with, share common risk factors with or are causes or outcomes of OA remains unknown. The association is dose-dependent in terms of the number of comorbidities, suggesting multimorbidity (28).

On the other hand, a systematic review on patients with osteoarthritis reported worsening pain and reduced functional activities in these patients due to the presence of other chronic diseases (36). From the clinical point of view, comorbidities create more challenges in the treatment of osteoarthritis. The severity and burden in multimorbid patients is related to the number and pattern of different comorbid conditions. (37). However, except for shared risk factors such as aging and obesity, there is incomplete biological information regarding osteoarthritis and associated comorbidities. According to the European League Against Rheumatism (EULAR) and National Institute for Health and Care Excellence (NICE), for best practice, diagnosis and treatment of specific comorbidities and understanding their patterns in osteoarthritis are important and recommended (38).

The results of present study also showed a significant positive correlation between hypertension and one subscale of KOOS "other symptoms". Different studies reported a positive association between hypertension and OA (39). Lo et al. reported that metabolic factors namely hypertension, blood glucose levels, and elevated cholesterol may be associated with KOA independent of obesity, which might explain the relationship between KOA and hypertension (40).

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Our findings showed that gender had significant positive correlation with two subscales of KOOS including “other symptoms” and “sport and recreations function” in elderly. Some studies previously examined association between gender and OA (3, 4, 41). Elderly women had a higher risk of having KOA and hand OA while men were more susceptible for spine OA (41). KOA is more severe and debilitating in women than in men (3), possibly because of low cartilage volume, and general differences in biomechanics between men and women.

Conclusion

Iranian elderly people with KOA outcomes are likely to have risk factors such as frequent joint use, obesity, as well as diabetes and multimorbidity. The multiplicity of chronic diseases and their impact on management decisions can complicate the KOA outcomes. Comorbidities increase the complexity of care through increased drug exposure and other chronic conditions. Although managing the risk factors and proper intervention of chronic diseases can reduce the adverse impacts of KOA, more studies are needed on comorbidity in OA regarding the etiology of this relationship and clinical implications. Also, it is necessary that future works target guidelines of prevention of KOA outcomes by focusing on lifestyle modification among elderly populations.

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