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Association between conicity index (C-index), relative fat mass (RFM), and osteoarthritis (OA): evidence from NHANES 2003–2018

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Abstract

Background Obesity is considered an important risk factor for osteoarthritis (OA), with conicity index (C-index), relative fat mass (RFM) are two novel anthropometric measures of obesity. To investigate the association between OA and these two indicators, we conducted this study.

Methods We used data from the National Health and Nutrition Examination Survey (NHANES) to investigate the association between C-index, RFM, and OA. First, the participants were divided into two groups according to whether they had OA, and we compared the baseline characteristics of the two groups. Then, C-index and RFM were divided into quartiles (Q1, Q2, Q3, Q4) for multivariate regression analysis. Additionally, we applied restricted cubic spline (RCS) to assess whether the relationship is non-linear. Finally, we conducted a subgroup interaction analysis to investigate whether this relationship varies across different subgroups.

Results The study included 34,707 participants, with a weighted OA prevalence of 7.7%. Significant differences in C-index and RFM were observed between OA and non-OA groups. Treating C-index and RFM as categorical variables, logistic regression showed significantly higher OA risk in Q4 compared to Q1: for C-index, Q4 (OR = 1.60; 95% CI: 1.33–1.93; $P < 0.001$); for RFM, Q4 (OR = 2.07; 95% CI: 1.57–2.73; $P < 0.001$). The RCS results show that the relationship between C-index and OA is non-linear, while the relationship between RFM and OA is linear. Subgroup interaction analysis showed some interaction effects.

Conclusions This study reveals detailed relationships between C-index, RFM, and OA, which may be better indicators of obesity in assessing OA risk.

Keywords Osteoarthritis, C-index, RFM, NHANES

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Background

Osteoarthritis (OA) is a degenerative joint disease, which can cause joint pain, swelling and stiffness, affecting a person's move ability [1]. The main pathological changes of osteoarthritis include cartilage degeneration, subchondral bone remodeling, osteophyte formation, and synovial inflammation [2]. OA can affect multiple joints, with the knee, hand and hip joints being the most common [3]. Risk factors for OA include age, gender, race, and obesity, among which obesity is considered to be the most powerful modifiable factor [4]. In 2020, approximately 595 million individuals worldwide were affected by OA, representing a significant increase of 132.2% in total cases compared to 1990, and the prevalence of OA is expected to continue to rise by 2050 [5]. Currently, exercise and weight management are fundamental components in the treatment of OA. For patients with mild symptoms, oral nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular injections can provide symptomatic relief. However, in cases of advanced symptoms and structural damage, total joint replacement surgery is often a more appropriate intervention [6]. OA not only significantly impacts the physical and mental health of patients but also imposes a heavy socioeconomic burden. Therefore, how to prevent and manage OA is of great importance.

Obesity is widely recognized as a significant risk factor of OA, increasing its incidence and accelerating disease progression [7]. Over the past 50 years, global obesity prevalence has risen substantially, concurrently elevating the risks of comorbidities such as type 2 diabetes, hypertension, heart disease, and OA [8]. Obesity, hypertension, and other related diseases have been confirmed in previous studies to significantly impact the health of the musculoskeletal system [9–11]. Obesity not only increases the mechanical load in the weight-bearing region, but also correlates with the inflammatory immune responses in chondrocyte microenvironment [12]. Furthermore, obesity has been consistently linked to vitamin D deficiency. This deficiency may subsequently modulate serum oxidative stress markers in OA patients, potentially influencing both pain severity and joint function [13, 14]. A body mass index (BMI) of 25 or higher is commonly used to define overweight, while a BMI of 30 or higher is used to define obesity [15]. However, limitations exist in the use of BMI to define obesity. For example, it is unable to distinguish between fat and muscle mass or account for gender differences in fat distribution. Given the strong link between obesity and OA, focusing on BMI in OA research may lead to bias in clinical practice [16]. In fact, in response to the limitations of BMI in assessing obesity and predicting disease risk, researchers have developed new indicators such as weight-adjusted waist index (WWI) and body roundness index (BRI), which have demonstrated promising results [17–19]. The conicity index (C-index) and relative fat mass (RFM) are two novel measures that more accurately reflect the total body fat percentage. C-index and RFM are calculated from the anthropometric measurements of waist circumference (WC), height, and body weight, which are considered more effective than the BMI in the evaluation of obesity [20, 21]. Current research has yet to establish the relationships between C-index, RFM, and OA risk. Therefore, this study aims to investigate these associations and evaluate their potential as predictive tools for identifying high-risk OA populations.

Methods

Study population

Data from the National Health and Nutrition Examination Survey (NHANES, https://wwwn.cdc.gov/nchs/nhanes) were used in this cross-sectional study. NHANES is a sophisticated, multi-stage probabilistic sample survey carried out by the Centers for Disease Control and Prevention (CDC). Its purpose is to gather data on various health issues. NHANES conducts standardized questionnaire interviews, physical examinations, and laboratory tests, which is conducted by the Mobile Examination Center (MEC). Ethical approval for this survey was given by the Research Ethics Review Board (ERB) of the National Center for Health Statistics (NCHS). The data collected through NHANES is publicly accessible and is extensively utilized in epidemiological research, health assessments, and the formulation of health guidelines.

In this study, the participant sample was derived from eight NHANES cycles (2003—2018), encompassing a total of 80,312 individuals. Subsequently, we employed the following stringent exclusion criteria to select the study subjects: (1) Participants with other types of arthritis or lacking relevant data were excluded; (2) Participants under 20 years of age or those who were pregnant were excluded (Fig. 1). To address the missing data in the analysis, we used the 'mice' package to perform multiple imputation of the study variables (C-index and RFM) and covariates. Finally, this study included 34,707 participants.

OA assessment

A comprehensive review demonstrated a remarkably high level of agreement between self—reported OA and clinical diagnoses [22]. Diagnostic information regarding OA was gathered in NHANES through the utilization of two questions in the questionnaire. The first question was "Has a doctor or other health professional ever told you had arthritis?" Participants who provided positive responses were subsequently asked follow—up question:

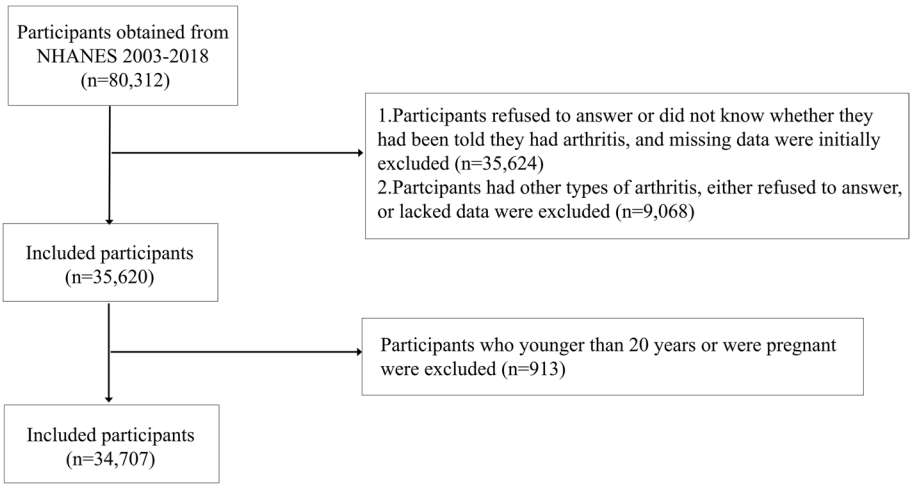

Fig. 1 The flowchart for the inclusion and exclusion of participants

"Which type of arthritis was it?" Finally, those participants who replied "osteoarthritis" were regarded as having OA and were included in our research.

C-index and RFM calculation

We utilized the following formulas for the calculation of the C—index and RFM [23]:

$$C-index = 0.109^{-1} \times WC(m) \times \left[\frac{weight(kg)}{height(m)}\right]^{-1/2}$$

$$RFMman = 64 - \left[20 \times \left(\frac{height(m)}{WC(m)}\right)\right]$$

$$RFMwoman = 64 - \left[20 \times \left(\frac{height(m)}{WC(m)}\right)\right]$$

Covariate assessment

In this study, variables associated with OA and obesity were included as covariates. These covariates included gender, age, race, poverty income ratio (PIR), marital status, educational level, presence of comorbidities, smoking exposure, alcohol consumption, and physical activity level. Age was categorized into three groups: 20—39 years old, 40—59 years old, and 60 years old and above. Race was classified into five categories: Mexican Americans, non—Hispanic Blacks, non—Hispanic Whites, non—Hispanic Asians, and other races. Marital status was divided into unmarried, living alone, and living with others. Educational level was grouped as below high school, high school graduate, and college or above. PIR was classified into three levels: < 1.3, 1.3—3.5, and > 3.5. Comorbidities encompassed diabetes (yes/no), depression (yes/no), hypertension (yes/no), and hyperlipidemia (yes/no). Smoking exposure was reflected by serum cotinine concentration. Alcohol consumption was classified as non—drinker, mild, moderate, and heavy based on the frequency and amount of alcohol intake by the participants [24]. Physical activity level was categorized as high and low according to the metabolic equivalent (MET) scores [25]. The classification criteria for the above—mentioned covariates are detailed in the Supplementary materials.

Statistical analysis

NHANES employs a complex multi—stage probability sampling framework. Thus, we analyzed data using the recommended weighting scheme per NHANES reporting guidelines to enhance the realism of survey estimates. In this study, the sample weights were calculated by dividing the 2-year MEC exam weight by the number of included cycles. During the analysis of baseline characteristics, continuous variables are presented as medians with interquartile ranges (M, IQR), and categorical variables are reported as counts (n) and percentages (%). To compare the differences in the included variables between the OA and non—OA populations, the Kruskal—Wallis test was utilized for continuous variables, and the Rao—Scott chi—square test was adopted for categorical variables. To examine the association between C-index, RFM, and OA risk, we performed binary multivariate logistic regression analysis. We divided the C—index and RFM into four levels, Q1, Q2, Q3, and Q4, according to quartiles. Among them, Q1, the lowest level, served as the reference group. Additionally, a trend test was conducted. Stepwise models were adopted to control for confounding variables: Model 1 (unadjusted), Model 2 (adjusted

for demographic and socioeconomic factors), Model 3 (with further adjustment for comorbidity status), and Model 4 (with additional adjustment for smoking, alcohol consumption, and physical activity). To investigate whether there is a non—linear relationship, we conducted a weighted Restricted Cubic Spline (RCS) analysis. Additionally, we performed a subgroup interaction analysis to determine whether the associations between C—index, RFM and OA vary across different subgroups. Finally, we compared the performance of these two indicators and BMI, in predicting the risk of OA by plotting the receiver operating characteristic (ROC) curve. Meanwhile, bootstrap tests for comparing correlated ROC curves are performed.

The analysis process was completed using R software (version 4.4.1). A two—sided *p*—value was adopted to determine significance, with the following threshold indications: *** represents $P<0.001$, ** represents $P<0.01$, * represents $P<0.05$.

Results

Baseline characteristics

The baseline characteristics of the participants are shown in Table 1. Altogether, 34,707 individuals participated in this study, representing 183,085,916 Americans. The weighted prevalence rate of OA population was 7.7%, respectively. Compared with the non—OA population, the OA population showed significant differences in age, gender, race, educational status, marital status, PIR and comorbidities ($P<0.05$). The weighted medians of C – index and RFM in the non—OA population were 1.29 and 33.40, respectively, while those in the OA population were 1.34 and 39.49, respectively. The C—index and RFM in the OA group were significantly higher than those in the non—OA group ($P<0.001$).

Multivariate logistic regression analysis

The results of the logistic regression revealed that higher C-index and RFM are associated with an increased risk of OA, and the results of the trend tests were all statistically significant (P for trend < 0.001). The relationship between the C—index and OA was shown in all four models: compared with the first quartile (Q1), both Q3 and Q4 exhibited significant differences and were positively correlated with the risk of OA. Among them, in the fully adjusted Model 4, Q4 showed the highest odds ratio (OR) value compared with Q1 ($P<0.001$), and the estimated OR value and its 95% confidence interval (CIs) were 1.60 (1.33–1.93). For RFM, all four models confirmed a positive correlation between RFM and OA, and the OR value corresponding to RFM increases significantly. Moreover, in Model 4, the most significant difference was shown between Q4 and Q1 ($P<0.001$; OR = 2.07, 95CI%: 1.57–2.73). The detailed results are presented in Table 2.

RCS

To investigate whether there was a non—linear relationship among the C—index, RFM, and OA, we conducted a weighted RCS analysis. As depicted in Fig. 2, the C—index and RFM were positively correlated with the risk of OA (knot = 4). Additionally, the relationship between the C—index and OA is non – linear (P-non-linear = 0.0007 < 0.05), while the relationship between RFM and OA is linear (P-non-linear = 0.5202 > 0.05). The RCS analysis of the other two knots (3 and 5) proves that the result is robust (Fig. S1- S2).

The relationships among the C—index, RFM, and OA were analyzed through the RCS method. The non-linear association was evaluated using the P-non-linear, and a P-non-linear < 0.05 was considered statistically significant.

Subgroup interaction analysis

To explore whether the associations among the C—index, RFM and OA varied depending on other covariates, we conducted a weighted subgroup interaction analysis. The subgroup analysis was stratified by all categorical variables. The results of the subgroup analysis showed that the correlation between the C—index and OA was affected by the age, race and hypertension (P values for interaction were < 0.05). Meanwhile, the relationship between RFM and OA was significantly influenced by diabetes, indicating the presence of an interaction (P values for interaction was < 0.05). The detailed results for each subgroup are presented in Table 3.

ROC results

To examine the performance of the C—index and RFM as predictors of OA, we plotted the ROC curves (Fig. 3). The results revealed higher AUC values for both C-index and RFM compared to BMI, validating the superior predictive performance of these novel metrics over conventional BMI for OA. To assess the robustness of the predictive performance, we performed Bootstrap resampling on the ROC analysis results. The statistical comparison revealed that both the C-index and the RFM exhibited statistically significant superiority over BMI (Table S1).

Discussion

In this cross—sectional study, we found significant differences between the OA group and the non-OA group in terms of C—index, RFM, age, race, gender, marital status, comorbidities, smoking, alcohol consumption, physical activity, etc. Multivariable logistic regression showed that both the C—index and RFM were positively correlated

Table 1 Weighted baseline characteristics of participants ($n = 34,707$)

Characteristics	Total population	Non-OA population	OA population	*p*-value
median [IQR] or N (%)	**34,707**	**92.3**	**7.7**	
Age, n (%)				< 0.001
20–39	42.9	45.8	7.2	
40–59	37.4	37.3	37.8	
> = 60	19.8	16.8	55	
Gender, n (%)				< 0.001
Male	50	51.1	36.3	
Female	50	48.9	63.7	
Race, n (%)				< 0.001
Mexican American	9.3	9.7	4.2	
Non-Hispanic Black	11.4	11.6	9.2	
Non-Hispanic White	65.4	64.3	78.6	
Other	8.1	8.4	4.8	
Other Hispanic	5.8	6.0	3.3	
Marital status, n (%)				< 0.001
alone	16.6	15.4	31	
live with others	62.7	62.7	61.8	
never married	20.7	21.9	7.2	
Educational status, n (%)				< 0.001
Below high school	15.9	15.6	19	
High School	23.4	23.2	26	
college	60.7	61.2	55.1	
PIR, n (%)				0.043
< 1.3	22.1	22.2	21.8	
1.3–3.5	35.2	35	38.2	
> 3.5	42.6	42.9	39.9	
Depression, n (%)				< 0.001
Yes	6.6	6.1	11.9	
No	93.4	93.9	88.1	
Diabetes, n (%)				< 0.001
Yes	10	9.2	20	
No	90	90.8	80	
Hypertension, n (%)				< 0.001
Yes	31.6	29.3	58	
No	68.4	70.7	42	
Hyperlipemia, n (%)				< 0.001
Yes	88.9	88.7	91.5	
No	11.1	11.3	8.5	
Physical activity, n (%)				< 0.001
High	30.4	31	23.8	
Low	69.6	59	76.2	
Alcohol consumption, n (%)				< 0.001
heavy	15.2	15.9	7	
mild	49.8	48.9	60.8	
moderate	23.1	23.6	16.7	
non-drinker	11.9	11.6	15.5	
cotinine (median [IQR])	0.04 [0.01, 15.11]	0.05 [0.01, 17.60]	0.04 [0.01, 1.03]	0.002
C-index (median [IQR])	1.29 [1.23, 1.36]	1.29 [1.23, 1.35]	1.34 [1.28, 1.40]	< 0.001
RFM (median [IQR])	33.80 [28.34, 41.34]	33.40 [28.09, 40.80]	39.49 [32.28, 45.34]	< 0.001

Continuous variables are displayed as weighted medians, categorical variables are displayed as weighted percentages

Table 2 Logistic regression Results

Models	Model 1	Model 2	Model 3	Model 4
C-index OR (95%CI)				
Q1	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
Q2	1.61 (1.33–1.94) ***	1.20 (0.99–1.45)	1.17 (0.96–1.42)	1.17 (0.97–1.42)
Q3	2.78 (2.36–3.27) ***	1.59 (1.32–1.90) ***	1.47 (1.22–1.78) ***	1.49 (1.23–1.80) ***
Q4	4.45 (3.81–5.20) ***	1.83 (1.53–2.18) ***	1.58 (1.31–1.90) ***	1.60 (1.33–1.93) ***
P trend	< 2E-16	6.01E-12	2.93E-07	1.26E-07
RFM OR (95%CI)				
Q1	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00(ref)
Q2	2.03 (1.64–2.50) ***	1.40 (1.12–1.74) **	1.30 (1.04–1.62) *	1.31 (1.05–1.65) *
Q3	2.52 (2.07–3.08) ***	1.69 (1.32–2.16) ***	1.48 (1.15–1.89) **	1.50 (1.17–1.92) **
Q4	4.52 (3.74–5.48) ***	2.50 (1.92–2.26) ***	2.03 (1.55–2.67) ***	2.07 (1.57–2.73) ***
P trend	< 2E-16	7.52E-13	2.96E-08	2.47E-08

Model 1: unadjusted model

Model 2: adjusted for age, gender, race, marital status, PIR, and education level

Model 3: adjusted for variables of model 2 and comorbidities status

Model 4: adjusted for variables of Model 3, alcohol consumption, smoking exposure and physical activity

* $P < 0.05$

** $P < 0.01$

*** $P < 0.001$

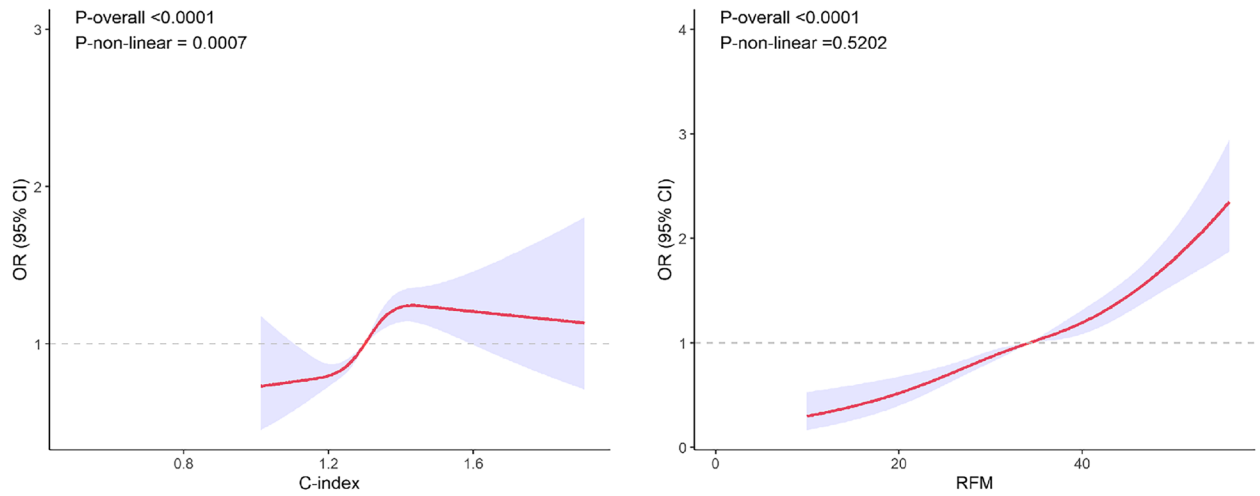

Fig. 2 RCS results of C-index and RFM (knot = 4)

with the risk of OA. The RCS analysis indicated that there was a significant non—linear positive correlation between the C—index and the risk of OA, while the relationship between RFM and the risk of OA was linearly positive. Subgroup interaction analysis further found that the relationship between C-index and OA was influenced by age, race and hypertension, while diabetes interacted with the relationship between RFM and OA. However, the subgroup interaction results are exploratory and require further verification. Finally, the ROC curve confirmed that the C—index and RFM were superior to BMI as predictors.

OA significantly impairs patients' quality of life and mobility and obesity is considered a key modifiable risk factor for it [26]. Numerous studies have confirmed the roles of various obesity indicators, such as BMI, WC, fat mass and muscle mass measured by dual—energy X—ray absorptiometry, in increasing the risk of OA, promoting its progression, and aggravating OA symptoms [27–29]. The above evidence indicates the necessity of detecting

Table 3 Subgroup analysis and interaction results

Characteristic	C-index (quartile)	RFM (quartile)
	OR (95%CI)	OR (95%CI)
Gender		
Male	1.33 (1.20, 1.47)***	1.33 (1.20, 1.49)***
Female	1.10 (1.03, 1.17) **	1.26 (1.12, 1.41)***
P for interaction	0.229	0.663
Age		
> =60	1.12 (1.05, 1.20)**	1.25 (1.13, 1.37)***
40–59	1.18 (1.08, 1.29)***	1.26 (1.10, 1.46)***
20–39	1.25 (1.07, 1.48)**	1.65 (1.32, 2.06)***
P for interaction	0.023	0.093
Race		
Mexican American	1.38 (1.17, 1.62)***	1.38 (1.13, 1.69)**
Non-Hispanic Black	1.21 (1.10, 1.34)***	1.56 (1.36, 1.78)***
Non-Hispanic White	1.13 (1.06, 1.20)***	1.24 (1.13, 1.36)***
Other	1.38 (1.08, 1.77)*	1.47 (1.03, 2.09)*
Other Hispanic	1.45 (1.21, 1.74)***	1.48 (1.10, 1.99)**
P for interaction	0.019	0.631
Depression		
Yes	1.05 (0.91, 1.21)	1.35 (1.09, 1.68)**
No	1.18 (1.11, 1.25)***	1.28 (1.18, 1.39) ***
P for interaction	0.155	0.127
Diabetes		
Yes	1.17 (1.03, 1.34)*	1.46 (1.21, 1.75) ***
No	1.15 (1.09, 1.22)***	1.27 (1.16, 1.38)***
P for interaction	0.338	< 0.001
Hypertension		
Yes	1.12 (1.04, 1.20)**	1.24 (1.12, 1.38)***
No	1.20 (1.11, 1.29)***	1.33 (1.19, 1.50) ***
P for interaction	0.022	0.149
Hyperlipemia		
Yes	1.16 (1.10, 1.23)***	1.28 (1.18, 1.39)***
No	1.17 (0.98, 1.41)	1.34 (1.03, 1.74)*
P for interaction	0.563	0.989
Physical activity		
High	1.22 (1.10, 1.35)***	1.42 (1.21, 1.67)***
Low	1.15 (1.08, 1.22)***	1.24 (1.14, 1.36)***
P for interaction	0.267	0.185
Alcohol consumption		
Heavy	1.08 (0.90, 1.30)	1.19 (0.94, 1.50)
Moderate	1.21 (1.07, 1.38)**	1.31 (1.07, 1.60)**
Mild	1.19 (1.11, 1.28)***	1.28 (1.15, 1.41)***
Non-drinker	1.07 (0.95, 1.22)	1.35 (1.12, 1.62)**
P for interaction	0.437	0.188

A *P* value for interaction < 0.05 indicates the presence of an interaction and the subgroup analysis was conducted under the fully adjusted Model 4

* *P* < 0.05, ** *P* < 0.01, and *** *P* < 0.001

obesity for OA prevention and alleviation. Although there are so many indicators available for selection, they all have inherent limitations. For example, BMI cannot reflect the proportion of fat and muscle content, waist circumference only reflects abdominal obesity [30], and although using dual—energy X—rays to measure fat distribution is effective, few people undergo this examination. As two novel indicators, C—index and RFM also measure obesity using simple and easily accessible body measurement indicators and can overcome the above—mentioned limitations. Nevertheless, the relationship between them and OA has not been studied yet. Consequently, this study investigated the relationships among the C—index, RFM, and OA to gain a deeper understanding of the impact of obesity and fat distribution on the onset of OA. In the field of research exploring the correlations with various diseases, the C—index and RFM have been widely applied. For example, the associations between the C—index, RFM and type 2 diabetes have been investigated in a previous study. Both the C—index and RFM have exhibited outstanding predictive capabilities [23]. Additionally, the study by Jiang et al. has shown that an increase in the C—index level significantly elevates the risk of gallstones [31]. A large—scale population study has found that RFM is associated with depression, suggesting that paying attention to RFM may be beneficial for depression research [32]. This study has also successfully explored and validated the relationships among the C—index, RFM and OA.

The pathogenesis of OA is intricate, and the molecular mechanisms underlying OA remain unknown [33]. Currently, there have been numerous studies on how obesity affects the occurrence and development of OA. Previous studies have indicated that mechanical load is a crucial influencing factor, which increases the mechanical load on weight-bearing joints (such as the knee and hip) [34]. Mechanical overloading induces alterations in the structure and properties of articular cartilage. Consequently, these changes lead to modifications in the subchondral bone and a narrowing of the joint space, thereby accelerating the progression of OA [35]. Currently, research has shown that in patients with hand OA, a higher BMI is associated with more severe hand pain [36]. However, the mechanical load theory does not adequately account for how obesity influences the progression of OA in non-weight-bearing joints, such as the hands. This indicates that obesity may impact OA through alternative mechanisms.

Obese patients often suffer from adipose tissue dysfunction. Locally, adipose tissue can promote the destruction of cartilage matrix and exacerbate pain by secreting pro—inflammatory cytokines (such as IL—1β, IL—6, TNF—α, etc.) and adipokines (leptin, adiponectin,

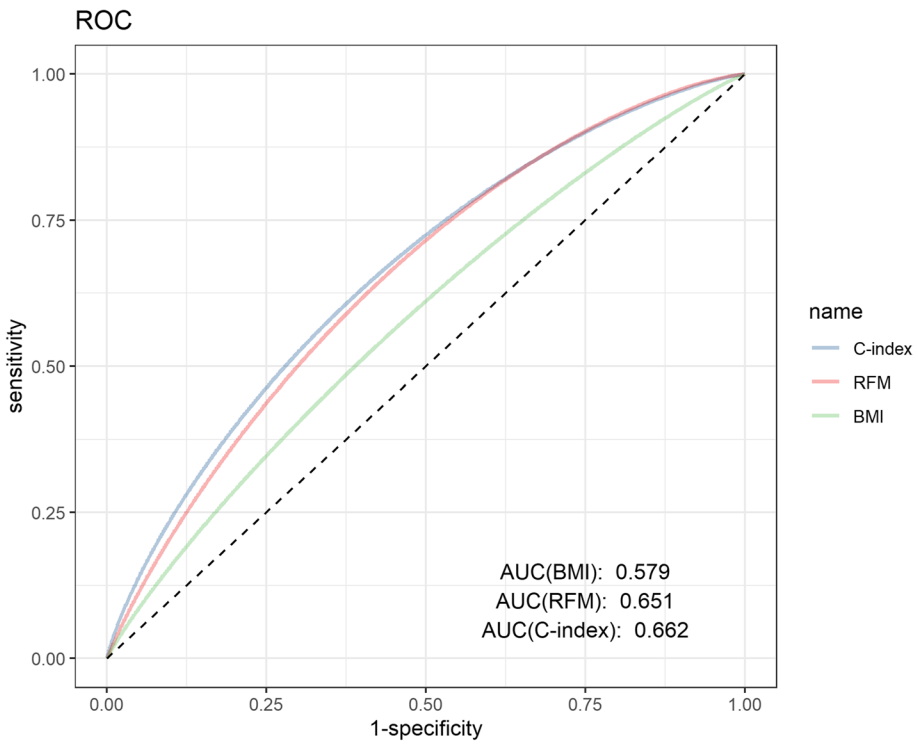

Fig. 3 ROC curves of C-index and RFM

adipokine resistin, etc.). The molecular mechanism involves the activation of NF-κB/JNK pathway, up-regulation of MMPs/ADAMTS to degrade cartilage matrix, polarization of M1 macrophages and dyslipidemia (cholesterol, ox-LDL) to exacerbate inflammation and cartilage destruction, and synergies to promote synovitis and osteopathy formation. Systemically, dyslipidemia in obese patients is associated with the amplification of joint inflammation, increased matrix catabolism, enhanced chondrocyte apoptosis, and a decreased pain threshold [37, 38]. Tang et al. 's study suggested that obesity and aging may promote multi-tissue cell aging through interaction, trigger systemic inflammation and immune microenvironment disorder, and further increase the severity of OA [39]. A review has indicated that gut microbiota dysbiosis is regarded as a crucial factor in the development of obesity—related OA in animal models. The mechanism summarized is that obesity gives rise to gut microbiota disturbances. Subsequently, gut microorganisms, their components, and microbiota—related lipid metabolites influence the progression of OA through interactions with the innate immune system at both the systemic and local levels [40]. In conclusion, obesity may affect OA through aspects such as mechanical overload, systemic inflammation, metabolic disorders, and gut microbiota dysbiosis. However, the complex mechanisms involved still require further investigation.

Strength

Our research utilizes two novel metrics to investigate their associations with OA. To the best of our knowledge, such an exploration has never been conducted previously. In terms of obesity assessment, these two indices take into account the distribution of adipose tissue and gender differences, addressing the drawbacks of traditional indices. The study population in our research is large and consists entirely of native Americans. This enables us to draw reliable and robust conclusions. The results of the logistic regression clearly demonstrate the correlations between these two indices and OA. The RCS successfully validates whether the relationship is linear. Furthermore, the ROC curve indicates the superiority of these two indices in evaluating OA. Finally, the subgroup stratified analysis reveals that age, race, hypertension and diabetes may interact with obesity to influence the progression of OA. This could potentially provide directions for future research.

Limitation

We must acknowledge the following limitations of this study: First, compared with cohort studies, cross—sectional studies have a relatively poor ability to determine causal relationships and are prone to recall bias. Second, due to the limitations of the data itself, this study did not exclude OA caused by trauma, which may have

had impact on the results. Third, the OA data collected by the NHANES do not cover specific joints, so it is impossible to conduct a stratified study on OA of different joints. Finally, the conclusions drawn from this study still require further experimental and clinical research to explore the specific mechanisms. Acknowledging these limitations can better explain our findings.

Conclusion

In conclusion, our study has identified a significant positive correlation among the C—index, RFM, and OA. Moreover, the predictive performance of the C—index and RFM for OA is superior to BMI. This finding emphasizes the necessity of providing weight loss education to individuals with high C—index and RFM values for the prevention of OA. However, these results necessitate further validation through larger-scale prospective studies to confirm their generalizability and robustness across diverse populations.

Abbreviations

OA	Osteoarthritis
NSAIDs	Nonsteroidal anti-inflammatory drugs
BMI	Body mass index
WC	Waist circumstance
C-index	Conicity index
RFM	Relative fat mass
NHANES	National Health and Nutrition Examination Survey
CDC	Centers for Disease Control and Prevention
NCHS	National Center for Health Statistics
ERB	Ethics Review Board
MEC	Mobile Examination Center
PIR	Poverty income ratio
MET	Metabolic equivalent
RCS	Restricted cubic spline
ROC	Receiver operating characteristic

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12944-025-02558-x.

Supplementary Material 1.

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Authors' contributions

R.X. conceived and designed the study. R.X. conducted the main analysis. W.J. acquired and processed the data. Y.M. provided software and technical support. W.J., W.G., and R.H. interpreted and verified the results. X.K. and X.P. supervised the work. X.P. and Y.M. administered the project. X.K. made a great contribution in the revision of the article and all authors participated in drafting the article.

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Declarations

Data availability

The data used in this study is publicly available at https://www.cdc.gov/nchs/nhanes/.

Ethics approval and consent to participate

Not applicable.

Consent for publication

All authors approved this publication.

Competing interests

The authors declare no competing interests.

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References

1. Jang S, Lee K, Ju JH. Recent Updates of Diagnosis, Pathophysiology, and Treatment on Osteoarthritis of the Knee. Int J Mol Sci. 2021;22:2619.
2. Varela-Eirin M, Loureiro J, Fonseca E, Corrochano S, Caeiro JR, Collado M, Mayan MD. Cartilage regeneration and ageing: Targeting cellular plasticity in osteoarthritis. Ageing Res Rev. 2018;42:56–71.
3. Kloppenburg M, Namane M, Cicuttini F. Osteoarthritis. The Lancet. 2025;405:71–85.
4. Allen KD, Thoma LM, Golightly YM. Epidemiology of osteoarthritis. Osteoarthritis Cartilage. 2022;30:184–95.
5. GBD 2021 Osteoarthritis Collaborators. Global, regional, and national burden of osteoarthritis, 1990–2020 and projections to 2050: a systematic analysis for the Global Burden of Disease Study 2021. Lancet Rheumatol. 2023;5:e508–22. https://doi.org/10.1016/s2665-9913(23)00163-7.
6. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. JAMA. 2021;325:568–78.
7. Bliddal H, Leeds AR, Christensen R. Osteoarthritis, obesity and weight loss: evidence, hypotheses and horizons - a scoping review. Obes Rev. 2014;15:578–86.
8. Blüher M. Obesity: global epidemiology and pathogenesis. Nat Rev Endocrinol. 2019;15:288–98.
9. Song S, Cai X, Hu J, Zhu Q, Shen D, Heizhati M, Yang W, Hong J, Li N. Correlation between plasma aldosterone concentration and bone mineral density in middle-aged and elderly hypertensive patients: potential impact on osteoporosis and future fracture risk. Front Endocrinol (Lausanne). 2024;15:1373862.
10. Song S, Cai X, Hu J, Zhu Q, Shen D, Ma H, Zhang Y, Ma R, Yang W, Hong J, et al. Effectiveness of Spironolactone in Reducing Osteoporosis and Future Fracture Risk in Middle-Aged and Elderly Hypertensive Patients. Drug Des Devel Ther. 2024;18:2215–25.
11. Song S, Cai X, Hu J, Zhu Q, Shen D, Ma H, Zhang Y, Ma R, Zhou P, Yang W, et al. Serum Uric Acid and Bone Health in Middle-Aged and Elderly Hypertensive Patients: A Potential U-Shaped Association and Implications for Future Fracture Risk. Metabolites. 2025;15:15.
12. Wang T, He C. Pro-inflammatory cytokines: The link between obesity and osteoarthritis. Cytokine Growth Factor Rev. 2018;44:38–50.
13. Amirkhizi F, Ghoreishy SM, Baker E, Hamedi-Shahraki S, Asghari S. The association of vitamin D status with oxidative stress biomarkers and matrix metalloproteinases in patients with knee osteoarthritis. Front Nutr. 2023;10:1101516.
14. Glover TL, Goodin BR, King CD, Sibille KT, Herbert MS, Sotolongo AS, Cruz-Almeida Y, Bartley EJ, Bulls HW, Horgas AL, et al. A Cross-sectional Examination of Vitamin D, Obesity, and Measures of Pain and Function in Middle-aged and Older Adults With Knee Osteoarthritis. Clin J Pain. 2015;31:1060–7.

15. Elmaleh-Sachs A, Schwartz JL, Bramante CT, Nicklas JM, Gudzune KA, Jay M. Obesity Management in Adults: A Review. JAMA. 2023;330:2000–15.
16. Godziuk K, Hawker GA. Obesity and body mass index: Past and future considerations in osteoarthritis research. Osteoarthritis Cartilage. 2024;32:452–9.
17. Hu J, Cai X, Song S, Zhu Q, Shen D, Yang W, Hong J, Luo Q, Li N. Association between weight-adjusted waist index with incident stroke in the elderly with hypertension: a cohort study. Sci Rep. 2024;14:25614.
18. Liang H, Si W, Li L, Yang K. Association between body roundness index and osteoarthritis: a cross-sectional analysis of NHANES 2011–2018. Front Nutr. 2024;11:1501722.
19. Zhao J, Cai X, Hu J, Song S, Zhu Q, Shen D, Yang W, Luo Q, Yao X, Zhang D, et al. J-Shaped Relationship Between Weight-Adjusted-Waist Index and Cardiovascular Disease Risk in Hypertensive Patients with Obstructive Sleep Apnea: A Cohort Study. Diabetes Metab Syndr Obes. 2024;17:2671–81.
20. do Prado CB. Martins CA, Cremonini ACP, Ferreira JRS, Cattafesta M, Almeida-de-Souza J, Zandonade E, Bezerra O, Salaroli LB: Cut Points of the Conicity Index and Associated Factors in Brazilian Rural Workers. Nutrients. 2022;14:4487.
21. Woolcott OO, Bergman RN. Relative fat mass (RFM) as a new estimator of whole-body fat percentage — A cross-sectional study in American adult individuals. Sci Rep. 2018;8:10980.
22. Peeters GM, Alshurafa M, Schaap L, de Vet HC. Diagnostic accuracy of self-reported arthritis in the general adult population is acceptable. J Clin Epidemiol. 2015;68:452–9.
23. Wang D, Chen Z, Wu Y, Ren J, Shen D, Hu G, Mao C. Association between two novel anthropometric measures and type 2 diabetes in a Chinese population. Diabetes Obes Metab. 2024;26:3238–47.
24. Lai B, Jiang H, Gao R, Zhou X. Association between alcohol intake and bone mineral density: results from the NHANES 2005–2020 and two-sample Mendelian randomization. Arch Osteoporos. 2024;19:21.
25. MacGregor KA, Gallagher IJ, Moran CN. Relationship Between Insulin Sensitivity and Menstrual Cycle Is Modified by BMI, Fitness, and Physical Activity in NHANES. J Clin Endocrinol Metab. 2021;106:2979–90.
26. Forhan M, Gill SV. Obesity, functional mobility and quality of life. Best Pract Res Clin Endocrinol Metab. 2013;27:129–37.
27. Gill SV, Hicks GE, Zhang Y, Niu J, Apovian CM, White DK. The association of waist circumference with walking difficulty among adults with or at risk of knee osteoarthritis: the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2017;25:60–6.
28. Jiang L, Tian W, Wang Y, Rong J, Bao C, Liu Y, Zhao Y, Wang C. Body mass index and susceptibility to knee osteoarthritis: a systematic review and meta-analysis. Joint Bone Spine. 2012;79:291–7.
29. Zhang X, Pan X, Deng L, Fu W. Relationship between Knee Muscle Strength and Fat/Muscle Mass in Elderly Women with Knee Osteoarthritis Based on Dual-Energy X-Ray Absorptiometry. Int J Environ Res Public Health. 2020;17:573.
30. Sweatt K, Garvey WT, Martins C. Strengths and Limitations of BMI in the Diagnosis of Obesity: What is the Path Forward? Curr Obes Rep. 2024;13:584–95.
31. Zhang J, Liang D, Xu L, Liu Y, Jiang S, Han X, Wu H, Jiang Y. Associations between novel anthropometric indices and the prevalence of gallstones among 6,848 adults: a cross-sectional study. Front Nutr. 2024;11:1428488.
32. Zhu X, Yue Y, Li L, Zhu L, Cai Y, Shu Y. The relationship between depression and relative fat mass (RFM): A population-based study. J Affect Disord. 2024;356:323–8.
33. Tong L, Yu H, Huang X, Shen J, Xiao G, Chen L, Wang H, Xing L, Chen D. Current understanding of osteoarthritis pathogenesis and relevant new approaches. Bone Res. 2022;10:60.
34. Chen L, Zheng JJY, Li G, Yuan J, Ebert JR, Li H, Papadimitriou J, Wang Q, Wood D, Jones CW, Zheng M. Pathogenesis and clinical management of obesity-related knee osteoarthritis: Impact of mechanical loading. J Orthop Translat. 2020;24:66–75.
35. Sun AR, Udduttula A, Li J, Liu Y, Ren PG, Zhang P. Cartilage tissue engineering for obesity-induced osteoarthritis: Physiology, challenges, and future prospects. J Orthop Translat. 2021;26:3–15.
36. Gløersen M, Steen Pettersen P, Neogi T, Jafarzadeh SR, Vistnes M, Thudium CS, Bay-Jensen AC, Sexton J, Kvien TK, Hammer HB, Haugen IK. Associations of Body Mass Index With Pain and the Mediating Role of Inflammatory Biomarkers in People With Hand Osteoarthritis. Arthritis Rheumatol. 2022;74:810–7.
37. Binvignat M, Sellam J, Berenbaum F, Felson DT. The role of obesity and adipose tissue dysfunction in osteoarthritis pain. Nat Rev Rheumatol. 2024;20:565–84.
38. Sampath SJP, Venkatesan V, Ghosh S, Kotikalapudi N. Obesity, Metabolic Syndrome, and Osteoarthritis-An Updated Review. Curr Obes Rep. 2023;12:308–31.
39. Tang R, Harasymowicz NS, Wu CL, Choi YR, Lenz K, Oswald SJ, Guilak F. Gene therapy for fat-1 prevents obesity-induced metabolic dysfunction, cellular senescence, and osteoarthritis. Proc Natl Acad Sci U S A. 2024;121:e2402954121.
40. Liu Y, Ding W, Wang HL, Dai LL, Zong WH, Wang YZ, Bi J, Han W, Dong GJ. Gut microbiota and obesity-associated osteoarthritis. Osteoarthritis Cartilage. 2019;27:1257–65.

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