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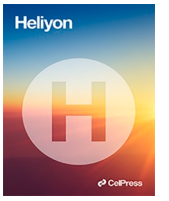

Research article

The correlation between frailty index and incidence, mortality in obstructive sleep apnea: Evidence from NHANES

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ABSTRACT

Background: The emergence of obstructive sleep apnea (OSA) is marked by a growing trend towards younger individuals, while its developmental trajectory remains shrouded in uncertainty, accompanied by intricate prognostic implications. While frailty and sleep problems often coexist, the relationship between them remains unclear. Hence, this study aims to utilize the National Health and Nutrition Examination Survey (NHANES) database from 2005 to 2008 to analyze and explore the relationship between the level of frailty index (FI) and the risk of OSA incidence and survival outcomes.

Materials and methods: Specialized weighted complex survey design analysis software was employed for data analysis. Multivariate logistic regression models and restricted cubic splines (RCS) were utilized to assess the association between FI and OSA incidence in all participants. Additionally, a Cox proportional hazards model was established to estimate the association between FI and the hazard ratios (HRs) for all-cause mortality and cardiovascular disease (CVD) mortality.

Results: A total of 8524 participants were included in this study. Compared to the Non-frail group ($FI \leq 0.1$), OSA risk increased with higher FI levels. In Model 3, adjusted for multiple covariates, the Pro-frail group ($0.1<FI \leq 0.2$) [odds ratio (OR) = 1.31, 95 % confidence interval (CI): (1.10, 1.56)], Mildly frail group ($0.2<FI \leq 0.3$) [OR = 1.62, 95 % CI (1.28, 2.05)], and Moderately/Severely frail group ($FI > 0.3$) [OR = 2.32, 95 % CI (1.55, 3.48)] exhibited an average 31 %, 62 %, and 132 % increase in OSA risk, respectively. RCS results demonstrated a nonlinear dose-response relationship between OSA risk and FI levels, with an increasing trend (P = 0.004). The Cox model indicated that, except for the Pro-frail group, OSA-related mortality risk also increased with higher FI levels, with a more pronounced effect on CVD-related mortality.

Conclusion: This study supports the hypothesis that FI may be associated with an increased risk of OSA, with a higher emphasis on OSA-related mortality risk in Mildly frail and Moderately/Severely frail populations.

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1. Introduction

With the growing awareness of the importance of sleep respiratory health, there is an increasing understanding of obstructive sleep apnea (OSA). Recurrent upper airway collapse is a defining feature of this condition, leading to chronic intermittent hypoxemia, changes in thoracic pressure, and disruptions in sleep structure. These factors can result in tissue hypoxia, oxidative stress, mitochondrial dysfunction, inflammation, and excessive sympathetic nervous system activation [1], and can even lead to severe consequences such as mortality [2]. Current treatment options for OSA are limited and often suboptimal, highlighting the significance of early diagnosis and effective prediction markers for OSA. This could help alleviate patient suffering, reduce healthcare costs, and provide a meaningful approach to managing OSA.

Frailty, traditionally considered a complex state associated with aging and physical decline, has now become an increasingly important health challenge due to the risk of its worsening in younger individuals, driven by societal stress and unhealthy lifestyles [3]. Previous research has explored the association between sleep behavior and frailty [4,5], suggesting a subtle connection between sleep and frailty, with implications for complications and mortality rates [6]. Some studies have indicated that aging may increase the risk of OSA [7,8], but the mechanisms behind this susceptibility remain unclear.

OSA is a progressively common and younger demographic in the spectrum of sleep disorders [9]. Due to its significant variability within the population [7], assessing OSA solely on a single aspect is considered unreliable. Currently available tools for OSA assessment are not precise enough and are complex [10], leading to unexpected onsets of the disease. Often, patients seek medical attention only when their condition has progressed to a severe stage, greatly impacting their quality of life and reducing their life expectancy. The concept of a frailty index is emerging, reflecting the degree of intrinsic aging in an individual [4]. Nevertheless, there is limited research exploring the correlation between frailty and OSA, and no studies have yet utilized this index to predict the incidence and survival risk of OSA. The aim of this study is to explore the correlation between the frailty index and the incidence of OSA and its associated mortality risk using data from the National Health and Nutrition Examination Survey (NHANES).

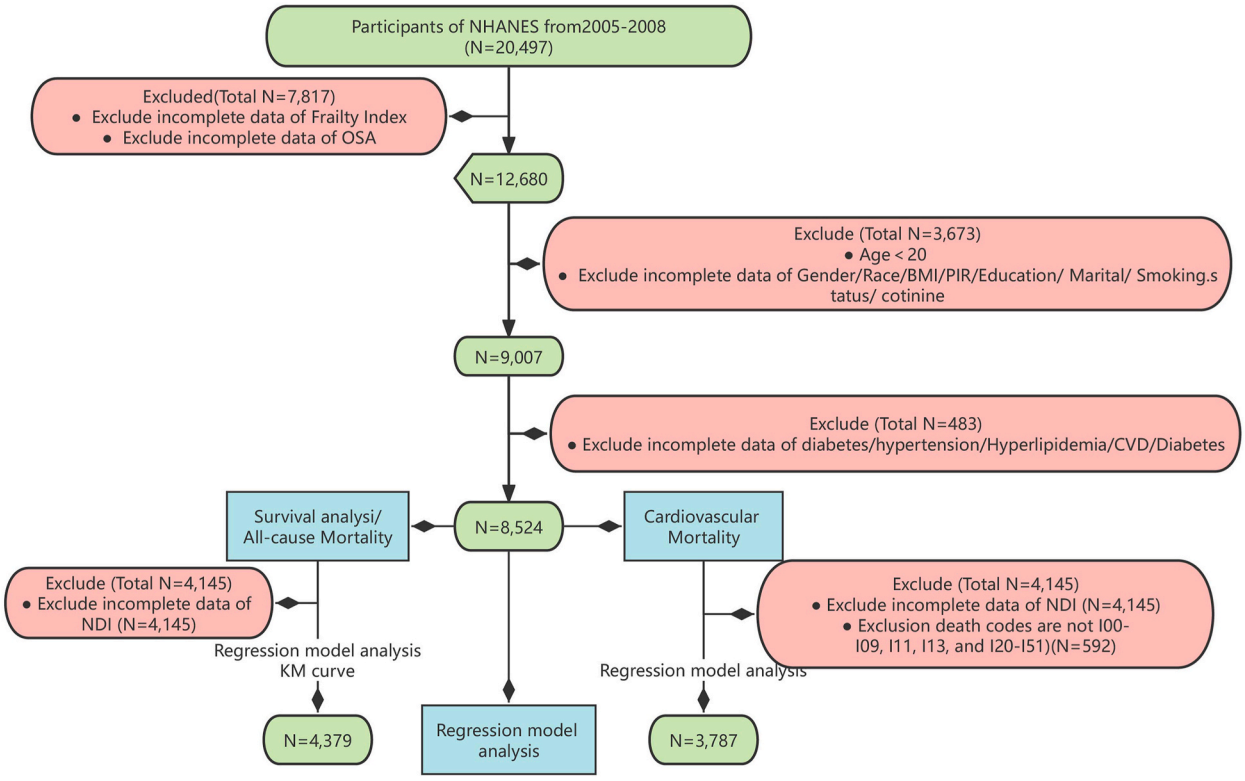

Fig. 1. Inclusion flow diagram.
In this study, missing data are considered as "random missing", and all exclusion criteria are based on the inclusion criteria. For example, the definition criteria for OSA were based on four questionnaire scales (SLQ120, SLQ030, SLQ070A, SLQ040), while frailty index were defined based on various scales and laboratory tests. Therefore, participants lacking these questionnaires and laboratory tests were excluded. In addition, the inclusion criteria for covariates are also detailed in the "Covariates" section, and similar exclusion criteria apply.
OSA: Obstructive sleep apnea; PIR: Poverty income ratio; CVD: Cardiovascular disease; BMI: Body mass index; NDI: National Death Index; KM: Kaplan-Meier.

2. Materials and methods

2.1. Study population in NHANES

We have identified the following reasons for excluding participants in our study: (1) Missing OSA; (2) Missing FI; (3) Aged under 20 years old; (4) Missing covariate data (e.g., hypertension, hyperlipidemia, diabetes); (5) Missing mortality data (Fig. 1A). All exclusion criteria are based on the absence of necessary questionnaires or laboratory tests for the included variables.

2.2. Definition of OSA

OSA was defined as follows [11,12]: (1) Self-report of being informed of having a sleep disorder (SLQ070A); (2) Frequent snoring (three nights or more per week) while sleeping (SLQ030); (3) Experiencing snorting, gasping, or cessation of breathing for three nights or more every week during sleep (SLQ040); (4) Feeling extremely sleepy during the daytime 16–30 times a month (SLQ120); (5) Experiencing one or more of the above symptoms.

2.3. Frailty index

Following the frailty standards set by Searle [13], Hakeem [14] expanded the criteria to include 49 deficits across various systems. These deficits encompass cognitive function (Memory lapses and cognitive challenges), dependency (difficulties in performing daily activities), depression (assessed using the PHQ-9), comorbidities (various chronic conditions), hospital visits, self-reported health compared to the previous year, physical abilities, body assessment (grip power and BMI), and laboratory results (including blood counts and glucose levels). The FI is calculated as the number of deficits a participant has divided by the total possible deficits, resulting in a numerical value between 0 and 1 (Supplementary material - Table S1). In accordance with previous research, individuals were categorized into four groups based on FI scores [15]: Non-frail ($FI \leq 0.1$), Pre-frail ($0.1<FI \leq 0.2$), Mildly frail ($0.2<FI \leq 0.3$), Moderately/Severely frail ($FI > 0.3$). The combination of moderate and severe frailty was due to the small proportion of severely frail individuals in the study sample (less than 0.5 %), following the approach of Jayanama [16].

2.4. Covariates

Our covariates are based on the following aspects: firstly, the demographic information of the respondents, including age, sex, and race. Secondly, there is information on the respondents' lifestyle and smoking behavior, the former including Body Mass Index (BMI) categorized as normal (<25 kg/m^2), overweight (≥ 25 kg/m^2, <30 kg/m^2), obese (≥ 30 kg/m2), Poverty Income Ratio (PIR) classified as low (≤ 1.39), medium (>1.39, ≤ 3.49), high (>3.49), as well as marital status and education level. Lastly, their underlying health conditions are also included, such as hypertension, hyperlipidemia [17], diabetes, and cardiovascular diseases (CVD). For detailed definitions of smoking and underlying health conditions, please refer to the supplementary materials - Table S2.

2.5. Mortality

The mortality rates of participants in this study were obtained through probabilistic matching using the National Death Index (NDI) up to December 31, 2019. This data was utilized to determine the all-cause mortality rates among the subjects in this research. Given the close association between OSA and cardiovascular mortality risk [2], this study also specifically explored the association between FI and cardiovascular mortality risk in OSA patients. Causes of death were identified using the International Classification of Diseases, Tenth Revision (ICD-10), with codes I00–I09, I11, I13, and I20–I51 being classified as cardiovascular disease-related causes of death.

2.6. NHANES analysis

The differences between OSA and non-OSA were assessed using weighted t-tests (for continuous variables) and weighted chi-square tests (for categorical variables). Continuous variables were displayed as the average value plus or minus the standard deviation (SD), whereas categorical variables were shown as the number of occurrences (N) and their corresponding percentages (%). Differences among the four groups based on FI classification were evaluated using Kruskal-Wallis tests (for continuous variables) or weighted chi-square tests (for categorical variables). This approach was presented by progressively adjusting covariates using a logistic regression model (crude model, model 1, model 2, model 3, model 4), and significant results were further subjected to subgroup analysis. Additionally, the interaction between FI and covariates on the significance of OSA was evaluated. Considering the presence of "random missingness" in the data values of this study, we employed multiple imputation (MI) techniques to fill in the missing data, aiming to address the potential for selection bias and repeated validations of its impact on the study outcomes, thereby enhancing the reliability of our conclusions. "Random forest imputations" were utilized for binary variables, while "Unconditional mean imputation" was employed for numerical variables.

Furthermore, the risk levels of all OSA variables were assessed by plotting forest plots. Following this, a calibration curve was generated to assess how well the predicted probabilities align with the actual proportions depicted in the forest plot. To further evaluate the performance of the constructed model, the area under the receiver operating characteristic (ROC) curve, known as the area under the ROC curve (AUC), was assessed. Decision curve analysis (DCA) was employed to determine the net benefit at various

probability thresholds and ascertain the model's suitability for clinical application [18]. Considering the influence of covariates, the restricted cubic splines (RCS) model provides a method for analyzing and visualizing the non-linear relationship between FI and OSA, and in this specific analysis, it was found to be statistically significant.

Kaplan-Meier survival curves with log-rank tests were employed to compare survival probabilities among OSA patients with different FI levels. Cox regression model was used to analyze the risk of death among patients in different frailty groups, adjusting covariates through multiple models. Statistical significance was determined for p-values below 0.05, with all probability tests reported being two-sided.

3. Results

3.1. Participant profile overview

A total of 8524 individuals were ultimately enrolled. After applying the selection criteria, 1559 participants were classified as having OSA. Compared to those without OSA (5210 individuals), OSA individuals exhibited a tendency to be of advanced age, had elevated FI levels, and represented a larger proportion of males, individuals with obesity, and smokers. Additionally, they exhibited a higher prevalence of hypertension, hyperlipidemia, diabetes, and CVD, irrespective of their income (as measured by PIR) or ethnicity (Table 1). These findings are consistent with the current health challenges faced by OSA patients. The nomograms graph visually represents these risk factors (Fig. 2A), and their reliability was confirmed by the calibration curve (Fig. 2B). The "baseline characteristics of the participants" in the data set after multiple imputations are generally consistent with the aforementioned conclusions (Supplementary Material - Table S2). When stratifying FI into Non-frail, Pro-frail, Mildly frail, and Moderately/Severely frail groups, it was noted that the proportion of OSA individuals increased with higher FI (Supplementary Material - Table S3).

Table 1
Characteristics of participants by OSA or Non-OSA. (NHANES 2005–2008, N = 8524).

Characteristic	Overall, N = 8524 (100 %)[a]	Non-OSA, N = 4145 (48 %)[b]	OSA, N = 4379 (52 %)[b]	P Value[3]
Age	46.1 (16.5)	44.9 (17.8)	47.3 (15.2)	**<0.001**
Sex				**<0.001**
Female	4443 (52 %)	2476 (61 %)	1967 (44 %)	
Male	4081 (48 %)	1669 (39 %)	2412 (56 %)	
Race				0.5
Non-Hispanic White	4214 (72 %)	2068 (71 %)	2146 (72 %)	
Non-Hispanic Black	1802 (11 %)	878 (11 %)	924 (11 %)	
Mexican American	1567 (8.0 %)	772 (8.2 %)	795 (7.7 %)	
Other Hispanic	597 (3.9 %)	249 (3.7 %)	348 (4.1 %)	
Other Race - Including Multi-Racial	344 (5.1 %)	178 (6.1 %)	166 (5.2 %)	
BMI				**<0.001**
Normal(<25)	2559 (33 %)	1623 (44 %)	936 (22 %)	
Obese(≥30)	3033 (33 %)	1062 (23 %)	1971 (44 %)	
Overweight(≥25,<30)	2932 (34 %)	1460 (33 %)	1472 (34 %)	
Education				**<0.001**
9-11th Grade (Includes 12th grade with no diploma)	1397 (12 %)	671 (12 %)	726 (13 %)	
College Graduate or above	1717 (27 %)	916 (29 %)	801 (24 %)	
High School Grad/GED or Equivalent	2043 (25 %)	930 (23 %)	1113 (26 %)	
Less Than 9th Grade	1020 (6.2 %)	470 (6.0 %)	550 (6.3 %)	
Some College or AA degree	2347 (30 %)	1158 (30 %)	1189 (31 %)	
Marital				**<0.001**
Divorced	4647 (58 %)	2025 (53 %)	2622 (63 %)	
Married	3601 (40 %)	1983 (45 %)	1618 (35 %)	
Never married	276 (2.4 %)	137 (2.4 %)	139 (2.4 %)	
PIR				0.2
High(>3.49)	2789 (45 %)	1324 (44 %)	1465 (46 %)	
Low(≤1.39)	2596 (20 %)	1296 (21 %)	1300 (20 %)	
Medium(>1.39,<=3.49)	3139 (35 %)	1525 (35 %)	1614 (34 %)	
Serum Cotinine (LBXCOT)	65 (134)	56 (125)	74 (141)	**<0.001**
Smoking status				**<0.001**
Current	1890 (23 %)	811 (20 %)	1079 (26 %)	
Former	2129 (24 %)	943 (23 %)	1186 (26 %)	
Never	4505 (52 %)	2391 (57 %)	2114 (48 %)	
Hypertension	3382 (35 %)	1406 (29 %)	1976 (40 %)	**<0.001**
Hyperlipidemia	6213 (72 %)	2867 (67 %)	3346 (76 %)	**<0.001**
Diabetes	1380 (12 %)	501 (8.4 %)	879 (15 %)	**<0.001**
CVD	7617 (92 %)	3776 (93 %)	3841 (91 %)	**<0.001**
Frailty Index	0.13 (0.09)	0.12 (0.08)	0.14 (0.09)	**<0.001**

[a] Mean ± SD for continuous; n (%) for categorical.
[b] *t*-test adapted to complex survey samples; chi-squared test with Rao & Scott's second-order correction.

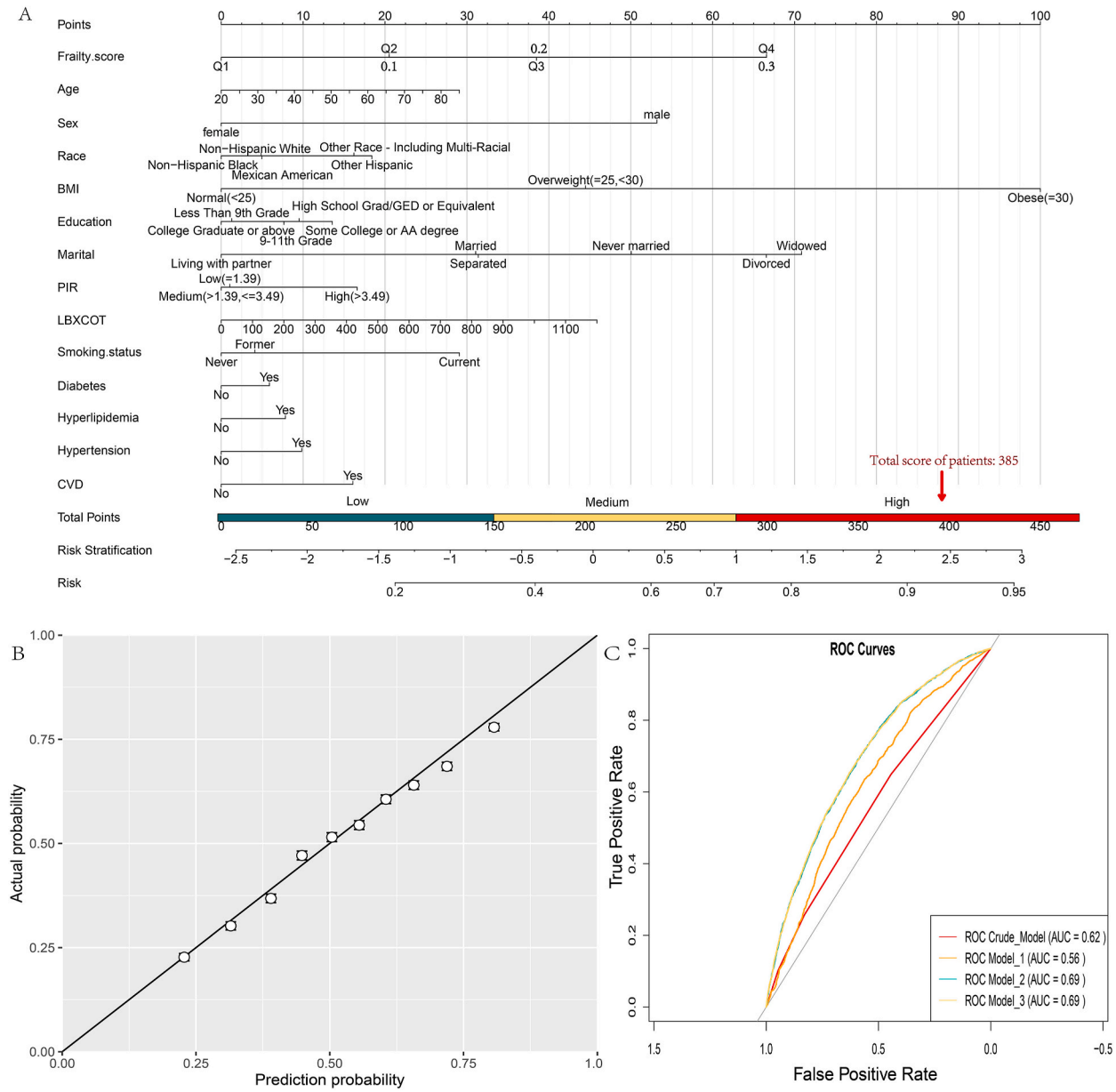

Fig. 2. (A) Nomograms for predicting OSA risk, used to assess the risk of depression based on Age, Sex, Race, Education, Marital status, PIR (Personal Income Ratio), BMI (Body Mass Index), serum cotinine, Smoking status, Hypertension, Hyperlipidemia, Diabetes. Each predictor has a score point, and the total score of these factors represents the likelihood of having OSA. For example, a 65-year-old female, Non-Hispanic Black, obese, with a high PIR, serum cotinine level of 800 (LBXCOT), current smoking status, along with hypertension, hyperlipidemia, diabetes, and no history of CVD, would have a score of 385 points (20 + 66+53 + 0+100 + 0+50 + 16+30 + 29+6 + 7.5+10 + 0 = 385), indicating a risk of OSA of over 90 %. (B) Calibration curves to validate the line chart. The X-axis represents the predicted probability, while the Y-axis represents the actual proportion. The diagonal solid line represents the best prediction of the ideal model, while the dots represent the deviation-corrected performance. The substantial overlap between these two parts demonstrates the reliability of the line chart. (C) Receiver Operating Characteristic (ROC) curves showing the ROC-AUC (Area Under the Curve) for the Crude model, Model 1, Model 2, and Model 3, which are 0.62, 0.56, 0.69, and 0.69, respectively.

3.2. Associations between FI and OSA outcomes

Using multiple linear regression models with Non-frail as the reference category, it was found in various models that Pro-frail, Mildly frail, and Moderately/Severely frail were all significantly positively associated with the risk of OSA ($P < 0.05$). This risk increased with higher FI levels, and the results remained robust after adjusting for covariates. Especially in Model 3, after adjusting for covariates, compared to the Non-frail group, the Pro-frail group [odds ratio (OR) = 1.31, 95 % confidence interval (CI): (1.10, 1.56)],

Mildly frail group [OR = 1.62, 95 % CI (1.28, 2.05)], and Moderately/Severely frail group [OR = 2.32, 95 % CI (1.55, 3.48)] exhibited average increases in the odds of having OSA by 31 %, 62 %, and 132 %, respectively. Furthermore, when analyzing using continuous variables instead of quartiles for FI, we can still obtain similar results (Table 2). Additionally, the data set after multiple imputations further validates the strong association between FI and the risk of OSA (Supplementary Material - Table S4). Further interaction analysis of the covariates presented in Table 1, which showed significant differences between OSA and Non-OSA, revealed that although differences persisted among most subgroups, there was no significant interaction between these covariates ($P > 0.05$), indicating the reliability of FI in predicting OSA risk (Table 3). The ROC curve demonstrated that the AUC for Model 3 was 0.69, indicating good predictive performance (Fig. 2C). The DCA curve depicted a net benefit probability of 0 %–80 % for Model 3, consistently exceeding the "None" group (as indicated by the solid black line), which indicates that compared to a model without any adjustments, our Model 3, which incorporates adjustments for multiple covariates, is less likely to produce false positives in exploring the association between FI and OSA risk, thus leading to greater benefits (Fig. 3A). Moreover, we applied RCS to analyze the relationship between FI and OSA and found a non-linear relationship after adjusting for covariates ($P = 0.004$, Fig. 3B).

During the 11–14 years of follow-up, Kaplan-Meier survival curves with log-rank tests showed that individuals with higher FI levels had a greater decrease in survival rates (Fig. 3C). During this period, the overall mortality rate among OSA patients reached 88 % (3635/4379), and after adjusting for multiple covariates, the Mildly frail [OR = 1.97, 95 % CI (1.37, 2.82)] and Moderately/Severely frail [OR = 3.02, 95 % CI (2.25, 4.05)] groups were significantly associated with all-cause mortality, with risks 1.97 and 3.02 times higher than that of the Non-frail group, respectively (Table 4). Additionally, FI was more strongly associated with cardiovascular-related mortality risk, with the Mildly frail [OR = 3.13, 95 % CI (1.13, 8.70)] and Moderately/Severely frail [OR = 5.03, 95 % CI (1.94, 13.0)] groups having risks 3.13 and 5.03 times higher, respectively, than that of the Non-frail group. When conducting mortality risk analysis with FI treated as a continuous variable and validating the data set after multiple imputations, these results are similar to those obtained using quartiles (Table 4, Supplementary Material - Table S5).

4. Discussion

To the best of our knowledge, this is a large-scale study investigating the incidence risk of OSA and its associated mortality risk in relation to frailty. The conclusions of this study align with our expectations, supporting a significant association between FI and both the risk of developing OSA and its mortality rate. Importantly, the association between FI and OSA risk appears to be non-linear and not influenced by other factors.

While the mechanisms between OSA and FI lack research, potential mechanisms may involve physiological and anatomical changes. Imaging studies have shown that the deposition of parapharyngeal fat and alterations in bone joints (resulting in a narrowing of the upper airway) are observed in aging populations [19,20]. Previous research has also noted increased airway resistance and reduced pharyngeal dilator muscle activity during sleep in older individuals [21]. Furthermore, disruptions in the immune system and neuroendocrine regulation cannot be overlooked. Patients with high FI often exhibit compromised immune systems, persistent chronic inflammation, elevated oxidative stress levels, and imbalances in growth hormone secretion [22], which may pose potential risks to survival [23]. Therefore, our study suggests that frailty prevention is necessary, especially for those with risk factors for OSA, such as chronic snoring, obesity, hypertension, high cholesterol, diabetes, and metabolic disorders [24]. Currently, most interventions for frailty combine nutritional supplements and specialized training [25], which is reasonable and necessary.

This study found that female subjects were more likely to experience Moderate/Severe frailty, possibly due to the fact that muscle strength in women declines faster than in men. Additionally, since women have a slightly longer life expectancy than men, there is a need to strengthen frailty prevention measures for women. As age is an important factor influencing FI, in subgroup analysis, we segmented age into young adults (20–30), middle-aged adults (31–45), middle-aged seniors (46–60), seniors (61–80), and elderly (over 80), while still adjusting for other covariates. We found that as age increased, the impact of age on the association with OSA weakened. Furthermore, the risk of OSA increased in patients with hypertension, high cholesterol, and diabetes, which may be related to metabolic diseases inducing OSA through mechanisms including anatomical and neural effects on the upper airway [26]. However, many of these factors did not have a decisive impact on association between FI and OSA in further interaction analysis.

Frailty has been shown to be associated with poor quality of life and an increased risk of all-cause hospitalization [27]. However,

Table 2
Multinomial logistic regression on the risk of FI and OSA in NHANES from 2005 to 2008.

Regression model	Crude Model OR (95 % CI)	Model 1 OR (95 % CI)	Model 2 OR (95 % CI)	Model3 OR (95 % CI)
Frailty Score				
Non-frail (FI ≤ 0.1]	Reference	Reference	Reference	Reference
Pro-frail (0.1<FI ≤ 0.2]	1.32(1.16, 1.50)[c]	1.46(1.27, 1.68)[c]	1.33(1.14, 1.55)[b]	1.31(1.10, 1.56)[a]
Mildly frail Q3 (0.2< FI ≤ 0.3]	1.68(1.46, 1.92)[c]	1.88(1.63, 2.18)[c]	1.65(1.36, 1.99)[c]	1.62(1.28, 2.05)[b]
Moderately/Severely frail Q4 (FI > 0.3)	2.37(1.79, 3.13)[c]	2.68(1.98, 3.64)[c]	2.28(1.67, 3.11)[c]	2.32(1.55, 3.48)[b]
Continuous variable	18.2(9.46, 35.1)[c]	35.3(17.2, 72.4)[c]	20.1(9.07, 44.7)[c]	23.8(8.13, 69.6)[c]

Model 1: Adjusted Age, Sex, Race; Model 2: Adjusted Age, Sex, Race, Education, Marital, PIR, Serum Cotinine, BMI, Smoking; Model 3: Adjusted Age, Sex, Race, Education, Marital, PIR, Serum Cotinine, BMI, Smoking, Hypertension, Hyperlipidemia, Diabetes, CVD.

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.001$.

Table 3
Subgroup analysis of the FI-related OSA risk after adjusting for various covariates.

Subgroup	Pro-frail (0.1<FI ≤ 0.2] OR (95%CI)	Mildly frail (0.2< FI ≤ 0.3] OR (95%CI)	Moderately/Severely frail (FI > 0.3) OR(95%CI)	Interaction P-value
Age				P = 0.08
20–30	1.57(1.09, 2.26)[a]	2.76(1.07, 7.12)[a]	1.71(0.16, 18.8)	
31–45	1.26(0.92, 1.73)	1.61(0.81, 3.22)	2.40(0.57, 10.1)	
46–60	1.09(0.77, 1.55)	1.67(1.09, 2.57)[a]	2.30(1.37, 3.86)[a]	
61–80	1.29(0.75, 2.22)	1.11(0.61, 2.04)	1.74(0.73, 4.16)	
>80	1.19(0.48, 2.92)	1.58(0.24, 10.3)	1.57(0.27, 9.01)	
Sex				P = 0.19
Female	1.42(1.10, 1.83)[a]	1.83(1.32, 2.53)[b]	3.02(1.87, 4.89)[b]	
Male	1.25(0.97, 1.61)	1.55(1.17, 2.05)[b]	1.43(0.98, 2.08)	
Education				P = 0.69
9-11th Grade (Includes 12th grade with no diploma)	1.23(0.87, 1.75)	1.67(0.92, 3.04)	1.52(0.77, 2.99)	
College Graduate or above	1.20(0.88, 1.65)	1.54(0.93, 2.57)	1.85(0.92, 3.71)	
High School Grad/GED or Equivalent	1.56(1.17, 2.08)[b]	1.93(1.38, 2.70)[b]	2.73(1.53, 4.86)[b]	
Less Than 9th Grade	1.09(0.66, 1.79)	1.34(0.78, 2.32)	3.34(1.64, 6.81)[b]	
Some College or AA degree	1.32(0.94, 1.85)	1.65(1.12, 2.43)[a]	2.47(1.42, 4.29)[b]	
Marital				P = 0.54
Divorced	1.30(1.07, 1.58)[a]	1.40(1.02, 1.91)[a]	2.44(1.32, 4.53)[a]	
Married	1.33(1.07, 1.65)[a]	1.63(1.26, 2.12)[b]	2.63(1.43, 4.84)[b]	
Never married	1.31(1.10, 1.56)[b]	1.74(1.32, 2.30)[b]	2.28(1.48, 3.52)[b]	
BMI (Kg/m^2)				P = 0.84
Normal(<25)	1.35(1.04, 1.76)[a]	1.71(1.13, 2.59)[a]	2.41(1.27, 4.56)[a]	
Obese(≥30)	1.18(0.88, 1.58)	1.63(1.08, 2.46)[a]	2.31(1.37, 3.88)[b]	
Overweight(≥25, <30)	1.39(0.98, 1.97)	1.44(0.79, 2.60)	2.09(1.21, 3.62)[a]	
Smoking status				P = 0.88
Current	1.32(0.94, 1.84)	1.72(0.99, 3.02)	2.07(1.12, 3.85)[a]	
Former	1.20(0.87, 1.65)	1.42(0.90, 2.23)	2.17(1.24, 3.79)[a]	
Never	1.33(1.07, 1.65)[a]	1.63(1.26, 2.12)[b]	2.63(1.43, 4.84)[b]	
Hypertension				P = 0.41
Yes	1.26(1.05, 1.51)[a]	1.68(1.14, 2.48)[a]	3.45(1.68, 7.10)[b]	
No	1.38(1.01, 1.89)[a]	1.54(1.15, 2.06)[a]	1.84(1.13, 3.00)[a]	
Hyperlipidemia				P = 0.61
Yes	1.32(0.88, 1.99)	1.76(0.90, 3.45)	2.76(1.44, 5.27)[b]	
No	1.29(1.07, 1.55)[a]	1.56(1.17, 2.07)[b]	2.23(1.40, 3.54)[b]	
CVD				P = 0.97
Yes	1.27(0.30, 5.35)	1.60(0.39, 6.56)	2.26(0.49, 10.5)	
No	1.31(1.10, 1.55)[b]	1.60(1.23, 2.07)[b]	2.17(1.38, 3.41)[b]	
Diabetes				P = 0.34
Yes	1.31(1.10, 1.56)[b]	1.74(1.32, 2.30)[b]	2.28(1.48, 3.52)[b]	
No	0.88(0.53, 1.47)	0.87(0.53, 1.44)	1.60(0.76, 3.34)	

Subgroup Analysis Adjustment Factors: Age; Sex; Race; Education; Marital; PIR; BMI; Serum Cotinine; Smoking status; Hyperlipidemia; Hypertension; Diabetes; CVD, excluding sub-group variables, and the reference object in the sub-group is Non-frail (FI ≤ 0.1]. Survival Time and Mortality Risk***P < 0.001.

[a] P < 0.05.

[b] P < 0.01.

there is currently limited research on relevant indicators concerning the mortality risk associated with OSA. This study demonstrates a strong correlation between FI and the mortality risk of OSA patients, enhancing the broad applicability of this indicator. Given the close association between OSA and severe CVD [28], we also analyzed the risk of cardiovascular-related mortality, which similarly demonstrated the effectiveness and higher accuracy of FI. Therefore, we should prioritize frailty in OSA patients, as interventions to reduce frailty burden may improve outcomes for these patients.

This work has certain limitations. Frailty may change dynamically, influenced by complex and variable factors. Despite our efforts to adjust for numerous variables, limitations may still exist. Then, because there is no standardized FI criterion, caution is needed when generalizing the conclusions of this study.

5. Conclusion

In conclusion, this study found that high FI (a novel indicator for assessing frailty) increases the risk of OSA and subsequent mortality risk. Even in the pre-frailty stage, there is an increased risk of OSA, though it does not affect the risk of mortality. However, Mildly frail and Moderately/Severely frail individuals have a significant impact on both. Further research is needed to validate the conclusions of this study.

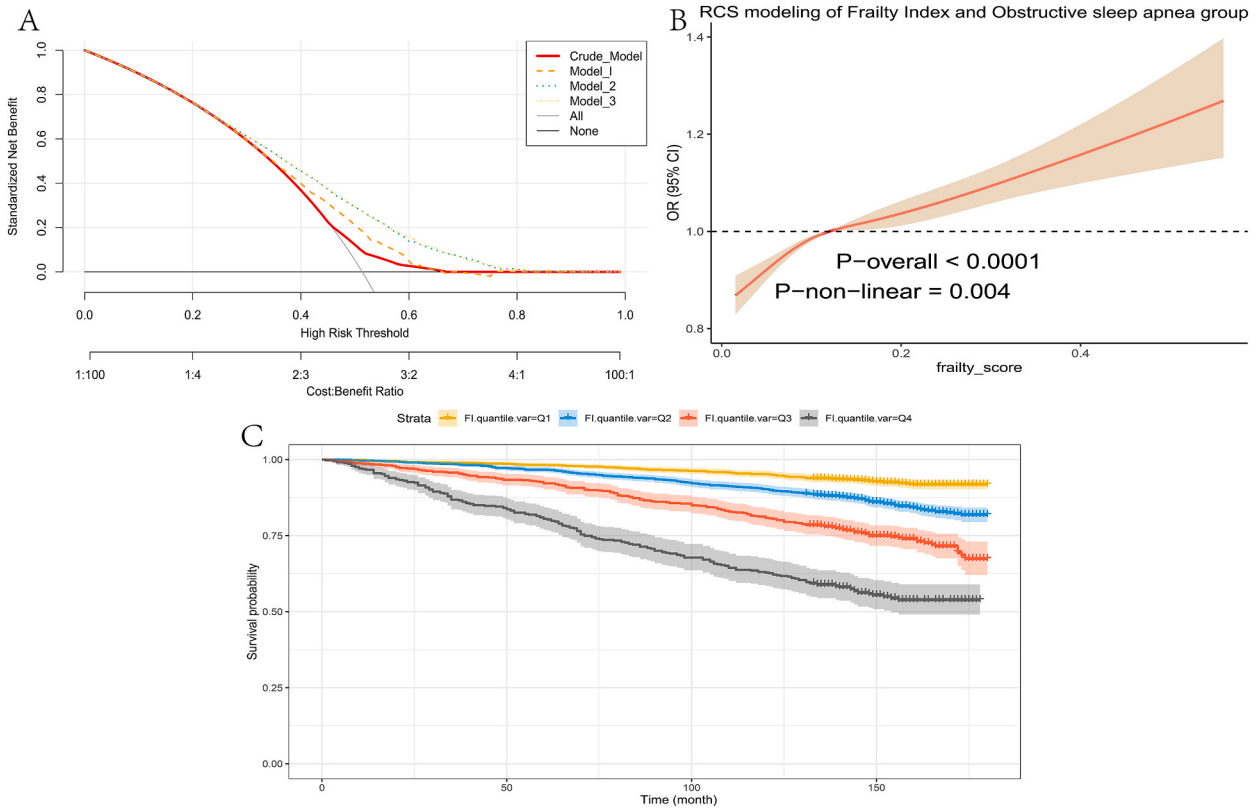

Fig. 3. (A) Decision Curve Analysis (DCA), showing the net benefit curves for various models. The X-axis represents the threshold probability for OSA, and the Y-axis represents the net benefit. The red line, orange line, light blue line, and yellow line represent the improved prediction curves of the Crude model, Model 1, Model 2, and Model 3, respectively. The gray line represents the assumption that all patients use the prediction curve model. The black line represents the assumption that no patients use the prediction curve model to predict the risk of depression. Our study indicates that all constructed models can provide more benefits for predicting an increased risk of OSA by lowering the net benefit threshold for these risk factors, and without producing side effects. (B) Adjusted using Restricted Cubic Spline (RCS) models for factors such as age, gender, race, PIR (Poverty Index), BMI, marital status, education level, smoking, hypertension, hyperlipidemia, coronary heart disease, diabetes, etc., analyzing the relationship between Frailty Index (FI) and OSA. The red solid line represents the combined restricted cubic spline curve model, and the shaded area represents the 95 % confidence interval of the combined curve. The dashed line represents the risk of Non-frail (FI $\leq$ 0.1) individuals developing OSA. (C) Kruskal-Wallis survival curve predicts the survival period of OSA patients at different FI levels, where Q1 (yellow) is for FI $\leq$ 0.1, Q2 (blue) is for 0.1<FI $\leq$ 0.2, Q3 (red) is for 0.2<FI $\leq$ 0.3, and Q4 (black) is for FI > 0.3. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Declarations

Ethics approval and consent to participate

The public database mentioned in this article contains raw data that has been approved by the NCHS Research Ethics Review Board, specifically the CDC NCHS National Health and Nutrition Examination Survey (NHANES) and the NCHS Ethics Review Board (ERB).

Data availability statement

The NHANES data in this study is sourced from the Centers for Disease Control and Prevention, and all data is freely accessible at: https://wwwn.cdc.gov/Nchs/Nhanes/

CRediT authorship contribution statement

Zhaoqi Yan: Writing – original draft, Software, Resources, Methodology, Investigation, Formal analysis, Data curation. **Yifeng Xu:** Software, Methodology. **Keke Li:** Resources, Methodology, Data curation. **Liangji Liu:** Writing – review & editing, Validation, Supervision.

Table 4
Exploring FI thresholds and mortality rates in OSA patients.

Mortality risk	Crude Model HR (95 % CI)	Model 1 HR (95 % CI)	Model 2 HR (95 % CI)	Model3 HR (95 % CI)
All-cause Mortality				
Non-frail (FI ≤ 0.1]	Reference	Reference	Reference	Reference
Pro-frail (0.1<FI ≤ 0.2]	2.1(1.57, 2.80)[c]	1.41(1.05, 1.90)[a]	1.39(1.09, 1.79)[b]	1.22(0.94, 1.59)
Mildly frail Q3 (0.2< FI ≤ 0.3]	4.74(3.35, 6.71)[c]	2.69(1.89, 3.84)[c]	2.48(1.81, 3.39)[c]	1.97(1.37, 2.82)[c]
Moderately/Severely frail Q4 (FI > 0.3)	10.1(7.56, 13.6)[c]	5.32(3.83, 7.37)[c]	4.36(3.23, 5.88)[c]	3.02(2.25, 4.05)[c]
Continuous variable	78.4 (34.2, 113.5)[c]	5.40 (4.7, 6.00)[c]	4.50 (3.8, 5.20)[c]	3.84 (2.00, 7.35)[c]
Cardiovascular Mortality				
Non-frail (FI ≤ 0.1]	Reference	Reference	Reference	Reference
Pro-frail (0.1<FI ≤ 0.2]	4.29(1.74, 10.6)[b]	2.56(1.05, 6.22)[a]	2.56(1.03, 6.38)[a]	2.04(0.85, 4.91)
Mildly frail Q3 (0.2< FI ≤ 0.3]	9.52(3.31, 27.3)[c]	4.65(1.69, 12.8)[b]	4.81(1.74, 13.3)[b]	3.13(1.13, 8.70)[a]
Moderately/Severely frail Q4 (FI > 0.3)	23.5(10.3, 53.4)[c]	10.7(4.18, 27.5)[c]	9.44(3.61, 24.7))[c]	5.03(1.94, 13.0)[c]
Continuous variable	72.4 (14.9, 352)[c]	40.5(10.11, 70.85)[c]	39.3(14.4, 64.5)[b]	6.22 (4.9, 9.52)[b]

Multiple logistic regression model: Model 1: Adjusted for Age, Sex, Race; Model 2: Adjusted for Age, Sex, Race, Education, Marital, PIR, Serum Cotinine, BMI, Smoking status; Model 3: Adjusted for Age, Sex, Race, Education, Marital, PIR, Serum Cotinine, BMI, Smoking status, Hypertension, Hyperlipidemia, Diabetes, CVD.

[a] $P < 0.05$.

[b] $P < 0.01$.

[c] $P < 0.001$.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e32514.

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