Plasma 25-hydroxyvitamin D level and risk of frailty among Chinese community-based oldest-old: evidence from CLHLS study

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Abstract

Background: Vitamin D deficiency has been linked to risk of frailty. However, there are limited data for evaluating the potential association of Vitamin D with frailty in a longevous (80+) population. The aim of this study was to examine the association between plasma 25-hydroxyvitamin D [25(OH)D] level and risk of frailty among Chinese oldest-old in the communities. Methods: Secondary analysis of data compiled by the 2011 wave of the Chinese Longitudinal Healthy Longevity Survey (n=1324) was extracted. Frailty was assessed by the Study of Osteoporotic Fractures (SOF) index. Multivariate logistic regression and spine smoothing with threshold effect analysis were performed to investigate the association between 25(OH)D level and risk of frailty after adjusting for socio-demographic variables, health characteristics and confounding biomarkers. Results: The mean age was 92.89 ± 7.92 years, and 844(63.7%) of participants were women. In all, 426 (33.2%, 95% confidence interval, CI: 29.66-34.69) frail participants were recorded . After adjustment for confounding covariates, the level of 25(OH)D was significantly related to frailty. By the spline smoothing with threshold effect analysis, a monotonically negative association between 25(OH)D and frailty was identified. Subgroup analyses revealed that the association did not differ by gender and age. Conclusions : 25(OH)D level was inversely associated with the risk of frailty among the Chinese community-based oldest-old.

Background

Frailty, as a geriatric syndrome, represents a reduced ability to re-build homeostasis in response to external stressors during daily life(1). Frailty in the elderly is well established to be related to long-term adverse health outcomes (such as falls, depression, disability, dependency, and mortality) which could not be completely explained by aging, function decline, or comorbidities (2-5).

Of existing numerous frailty measures, many often rely on measuring physical function with some being less likely to be readily available in clinical settings and therefore have limited use(6-8). Common approaches such as the Frailty Index(9, 10) and the Frailty Phenotype(11) are not exceptional. In contrast, the Study of Osteoporotic Fractures (SOF) frailty index, employed only 3 simple self-reported frailty components of muscle strengths, low energy, and unintentional weight loss(7). Frailty identified through this measure has been associated with falls, disability, fracture, and death(6, 12), and regarded as a useful tool for the physical aspects of frailty at the population level(7, 8, 13).

Vitamin D, which primarily synthesized in the skin upon the exposure to sunlight, is necessary for human's musculoskeletal health maintenance(14); its deficiency is proved to be the cause of muscle weakness(15), sarcopenia(16), falls(17), and fracture(18). A growing body of evidences have suggested that low level of its active form, namely 25-hydroxyvitamin D [25(OH)D], is related to risk of frailty(19-33). The underlying pathogenic mechanisms could be explained through 3 pathways: the first is the invalidation of regulatory effects of vitamin D on calcium flux, mineral homeostasis and protein anabolism in muscle tissue(23, 24); the second is bone metabolic disturbance by secondary hyperparathyroidism(25); the last is the possible property of vitamin D on anti-inflammation(26).

However, since the cutaneous synthesis of vitamin D shows great variability across populations(34), proofs of exploring its association in elderly Asian populations are limited. Moreover, as this cutaneous synthesis process decreases with age(35), and the limited outdoor activities may also accelerate vitamin D deficiency(14), the relationship between 25(OH)D and frailty in oldest-old people (aged≥80 years) remains unclear. Since the number of the oldest-old will be the fastest-growing group between now and 2050(11), the association between 25(OH)D level and risk of frailty in this age group may have important public health implications for health care planning and practice.

Therefore, this study aimed to examine the association between 25(OH)D level and risk of frailty among 1324 oldest-old adults of the eight longevity areas in the Chinese Longitudinal Healthy Longevity Survey (CLHLS)(36, 37). Given the evidences in previous studies, we hypothesized that lower level of 25(OH)D was associated with risk of frailty in the Chinese community-based oldest-old people.

Methods

Study design and participants

Participants with the biomarker sub-study datasets from the 6th (2011) waves of CLHLS were recruited in this secondary analysis. CLHLS is the first and largest nationwide, community-based, longitudinal prospective cohort survey, concerning older adults in China(38). It provides information on health status, socioeconomic characteristics, and lifestyles of the elderly, including a large percent of the oldest population(37). The in-depth study was launched in the eight longevity areas (Laizhou of Shandong Province, Xiayi of Henan Province, Zhongxiang of Hubei Province, Mayang of Hunan Province, Sanshui of Guangdong Province, Yongfu of Guangxi Autonomous Region, Chengmai of Hainan Province, Rudong of Jiangsu Province) (36). During the in-depth study, the Chinese Center for Disease Control and Prevention (CDC) local network medical doctors conducted physical examinations of the participants, and also collected biomarker datasets contain about 30 indicators on routine blood tests, blood biochemical tests, and urine tests (36). More detailed descriptions have been previously published elsewhere(39-41).

Initially, a total of 2439 elderly participants were included in the study. We excluded those of younger age (less than 80, n=834, 34.2%) and missing data on SOF index components (n=281, 11.5%). Finally, we retained 1324 older adults in this study.

Outcome

Consistent with previous studies of secondary analysis involving CLHLS data(42), frailty was defined by the SOF index in the current study. Three components were included in the index: underweight (defined as body mass index <18.5), low energy level (indicated by a positive response to the question “Over the last 6 months, have you been limited in activities because of a health problem?”), and muscle strengths (inability to stand up from a chair without the assistance of arms). As suggested, participants with two or more of the three components were defined as frailty.

Exposure

Fasting venous blood was collected after an overnight fast from all willing participants. Procedures for the collection and shipment of blood samples were described in detail elsewhere(14). 25(OH)D was assayed by an enzyme-linked immunoassay using Immunodiagnostic Systems Limited (IDS Ltd, Boldon, UK). The 25(OH)D level was expressed as nmol/L.

Covariates

We adjusted for socio-demographic variables, health characteristics and confounding biomarkers in the models. Socio-demographic variables included age, gender (female/male), marital status (married/other), residence (rural/other), education level (no schooling/≥1 years of schooling), co-residence [with family member(s) /other].

Health characteristics included lifestyles and chronic diseases. Lifestyles consisted of smoking (yes/no), drinking (yes/no), and regular exercise (yes/no) at present. Chronic diseases included hypertension (yes/no), diabetes mellitus (yes/no), heart diseases (yes/no), cerebrovascular diseases (yes/no), and respiratory diseases (yes/no). Hypertension was defined as systolic blood pressure≥140mmHg and/or diastolic blood pressure≥90mmHg(43). Diabetes mellitus was diagnosed by fasting plasma glucose≥7.0 mmol/L(14, 44). Other diseases were identified by self-report.

Confounding biomarkers were 11 indicators on blood routine tests and blood biochemistry tests (36). According to the previous relevant studies(19), these 11 indicators which largely investigated in relation with frailty were recruited in this study: 1) inflammatory marker: C reactive protein (CRP); 2) immune marker: counts of leukocytes (WBC); 3)clinical markers: plasma albumin (ALB), total cholesterol (CHO), serum creatinine (CREA), high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDLC), triglyceride (TG), and hemoglobin (HGB); 4) oxidative stress markers: malondialdehyde (MDA) and superoxide dismutase (SOD). All the standard laboratory techniques were performed by the central clinical lab at Capital Medical University in Beijing.

Overall, few data for most confounding variables were missing (1.05%). For the missing values, we did multiple imputations by chained equations to increase predictive power(45). Distribution of observed data and imputed data were described in **Supplementary Table S1 (see Additional file 1)**. For all the covariates, the distributions of observed and imputed values were similar.

Statistical Analysis

Categorical variables were expressed as numbers and percentages, and continuous data were described as mean (standard deviation, SD) or median (interquartile range, IQR). Characteristics among groups were compared by ANOVA, Kruskal–Wallis test or χ^2 test. The IQR of 25(OH)D level was used to divide the data into four categories. The cutoff points were 26.13, 35.89, 50.00 nmol/L.

We used multilayer logistic regression models based on the Likelihood Ratio Test (LRT) to determine the association between 25(OH)D level and the risk of frailty. Box-Tidwell method was used to test the linearity between logit P and all the continuous variables(46). Therefore, we used continuous terms for all the confounding biomarkers and categorized age as subgroups with 80-89, 90-99, ≥100 years. Data were reported as odds ratios (ORs) and 95% confidence intervals (CIs) in both unadjusted and adjusted logistic regression models. The *p*-value of Hosmer-Lemeshow test >0.05 indicated reasonable goodness of fit(47).

Different from previous studies, in order to examine the linear trend across levels of 25(OH)D, we further performed spline smoothing analysis and threshold effect analysis in the current study, which were relatively novel in studies of examining the respondents’ dose-response relationship between 25(OH)D and frailty. Instead of a priori assumptions, spline smoothing analysis is a form of mixture modeling based on the generalized additive model (GAM)(48), whereby a set of associated items, for example, 25(OH)D and frailty, can visually demonstrate the linear or curvilinear relationship by figures. As for the threshold effect analysis, which based on piece-wise regression model(49), can further examine whether this relationship is segmental or not.

Subgroup analyses and their interactions were tested to explore whether gender and age subgroups would confound the association between 25(OH)D level and frailly. Sensitivity analysis was performed in participants with complete variables, and multiple imputations, separately.

Two-tailed *p*-value <0.05 was considered the statistical significance in all the analyses. Statistical analyses were conducted by IBM SPSS Statistics Version 22.0, except for the spline smoothing analysis, threshold effect analysis, and multiple imputations were performed by R software Version 3.4.3 (http://www.R-project.org) and Empower® (www.empowerstats.com).

Table 1. Participant characteristics.

Variables	All participants (n=1324)	Categories (nmol/L)				statistics [a]
		Q_1 (≤26.13)	Q_2 (26.13–35.89)	Q_3 (35.89–50.00)	Q_4 (>50.00)	
Socio-demographics, n (%)						
Age (80-112), M (SD)	92.89(7.92)	95.63(7.49)	93.37(7.72)	91.85(7.85)	90.70(7.78)	25.207***
Female	844(63.7)	251(75.8)	236(71.3)	200(60.2)	157(47.6)	68.190***
Married	294(22.3)	44(13.3)	60(18.2)	83(25.1)	107(32.7)	40.503***
Rural	1124(84.9)	282(85.2)	282(85.2)	265(79.8)	295(89.4)	11.925**
No schooling	998(76.4)	279(85.8)	257(78.4)	242(74.2)	220(67.1)	33.410***
With household member(s)	950(73.2)	263(82.2)	236(72.2)	225(69.7)	226(69.1)	25.873***
Health characteristics, n (%)						
Smoking	148(11.3)	28(8.5)	39(11.8)	37(11.2)	44(13.5)	4.337
Drinking	167(12.7)	32(9.7)	41(12.5)	45(13.6)	49(14.9)	0.218
Regular exercise	178(13.9)	27(8.4)	38(11.9)	54(16.7)	59(18.6)	17.317***
Hypertension	785(62.2)	197(61.9)	195(62.1)	192(61.5)	201(63.0)	0.155
Diabetes mellitus	98(7.4)	28(8.5)	25(7.6)	24(7.3)	21(6.4)	1.057
Heart diseases	91(7.0)	24(7.4)	24(7.4)	27(8.4)	16(4.9)	3.398
Cerebrovascular diseases	102(7.8)	34(10.4)	31(9.5)	18(5.5)	19(5.8)	8.630*
Respiratory diseases	116(8.9)	29(9.0)	32(9.8)	23(7.0)	32(9.8)	2.080
Biomarkers, M (IQR)						
CRP (mg/L)	1.01(0.41,2.93)	1.12(0.38,3.35)	0.93(0.43,3.05)	0.96(0.41,2.54)	1.09(0.39,2.75)	1.491
ALB (g/L)	39.10(35.90,42.40)	37.90(35.30,41.40)	38.60(35.48,42.12)	39.70(36.70,42.93)	39.90(37.20,42.80)	29.923***
CHO (mmol/L)	4.16(3.52,4.79)	4.03(3.49,4.72)	4.21(3.51,4.79)	4.21(3.47,4.97)	4.20(3.70,4.78)	4.186
CREA (mmol/L)	78(65,96)	69(60,85)	77(63,93)	82(69,98)	87(71,102)	76.765***
HDLC (mmol/L)	1.23(1.03,1.49)	1.20(1.01,1.45)	1.25(1.04,1.51)	1.27(1.03,1.55)	1.23(1.04,1.46)	5.065
LDLC (mmol/L)	2.45(1.94,3.02)	2.40(1.92,2.97)	2.42(1.89,3.05)	2.41(1.86,3.08)	2.54(2.04,3.00)	5.147
TG (mmol/L)	0.79(0.59,1.10)	0.78(0.59,1.07)	0.79(0.58,1.09)	0.82(0.61,1.16)	0.77(0.57,1.07)	6.429
SOD (IU/mL)	58.53(53.43,63.24)	56.75(51.75,62.97)	58.18(53.49,63.20)	58.75(53.33,63.06)	59.39(55.39,64.24)	18.975***
MDA (μmol/L)	4.71(3.73,5.79)	4.81(3.93,5.89)	4.87(3.88,5.91)	4.84(3.82,5.83)	4.33(3.25,5.55)	27.303***
WBC (10^9/L)	5.30(4.30,6.40)	4.80(4.00,6.00)	5.10(4.10,6.10)	5.60(4.57,6.60)	5.60(5.60,6.80)	34.983***
HGB (g/L)	118(106,131)	121(110,133)	120(107,132)	116(105,129)	117(105,131)	11.618***

Frailty, n (%)	426(33.2)	162(48.9)	112(33.8)	93(28.0)	59(17.9)	76.606***

M (SD), mean (standard variance); M (IQR), median (interquartile range).

[a] Coefficient of ANOVA, Kruskal–Wallis test or χ^2 test among categories of plasma 25(OH)D level.

* <0.05, ** <0.01, *** <0.001.

Abbreviations: CRP, C reactive protein; ALB, plasma albumin; CHO, total cholesterol; CREA, plasma creatine; HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; SOD, superoxide dismutase; TG, triglyceride; SOD, superoxide dismutase; MDA, malondialdehyde; WBC, white blood cell count; HGB, hemoglobin.

Results

Sample characteristics

The Characteristics of participants were compared according to the categories of 25(OH)D level. The full detailed characteristics of all participants are shown in **Table 1**. The mean ± SD age of the study population was 92.89 ± 7.92 years, and 63.7% were women (n=844). Participants with frailty were 426 (33.2%, 95%CI: 29.66-34.69). The median 25(OH)D concentration was 35.89 nmol/L and participants with higher levels (35.89–50.00, >50.00 nmol/L) were significantly younger than those with lower levels (≤26.13, 26.13–35.89 nmol/L), more likely to be male, married, with ≥1 year of schooling and do regular exercise.

Association between the level of 25(OH)D and risk of frailty

As shown in **Table 1**, accounted for 48.9%, 33.8%, 28.0% and 17.9% of participants in the lowest to highest 25(OH)D categories reported frailty. There was a significant inverse association between categorical 25(OH)D level and risk of frailty in the multivariate logistic regression models. The ORs and 95% CIs for the association between categories of 25(OH)D level and frailty were presented in **Table 2**. After eliminating the interferences of all confounding factors, the ORs of frailty were 3.239 (95% CI: 2.113–4.967, p<0.001) for the lowest category (≤26.13 nmol/L) of 25(OH)D level, 2.341 (95% CI: 1.519–3.609, p<0.001) for the second-lowest (26.13–35.89 nmol/L), and 1.703 (95% CI: 1.088–2.664, p=0.20) for the third-lowest (30.33–44.46 nmol/L) compared to the highest level subgroup(>50.00 nmol/L), respectively.

Table 2. The associations between serum level of 25(OH)D (nmol/L) and risk of frailty.

Variables	Model 1 [a]	Model 2 [b]	Model 3 [c]	Model 4 [d, e]
Categories				
≤26.13	4.964(3.332,7.396) ***	3.472(2.273,5.303) ***	3.437(2.248,5.255) ***	3.239(2.113,4.967) ***
26.13–35.89	2.822(1.881,4.234) ***	2.414(1.571,3.710) ***	2.420(1.573,3.723) ***	2.341(1.519,3.609) ***
35.89–50.00	1.835(1.204,2.797) **	1.526(1.102, 2.683) *	1.722(1.102,2.692) *	1.703(1.088,2.664) *
>50.00	reference	reference	reference	reference

[a] Unadjusted model, OR (95%CI).

[b] Adjusted for **socio-demographics** (age, gender, marital status, residence, education level, and co-residence), OR (95%CI).

[c] Adjusted for **socio-demographics** (age, gender, marital status, residence, education level, and co-residence) and **health characteristics** (smoking, drinking, regular exercise, hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, and respiratory diseases), OR (95%CI).

[d] Adjusted for **socio-demographics** (age, gender, marital status, residence, education level, and co-residence), **health characteristics** (smoking, drinking, regular exercise, hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, and respiratory diseases) and **confounding biomarkers** (CRP, ALB, CHO, CREA, HDLC, LDLC, TG, SOD, MDA, WBC, and HGB), OR (95%CI).

[e] *p*-value for the Hosmer-Lemeshow test was 0.653, prediction in accuracy was 74.3% in model 4.

* <0.05, ** <0.01, *** <0.001.

The dose-response relationship between the level of 25(OH)D and the risk of frailty

Consistent with results displayed in **Table 2**, a continuous negative curve was observed between 25(OH)D and risk of frailty in the analysis using spline smoothing (*p* for trend <0.001, **Figure 1**). **Table 3** showed that the *p*-value of the log-likelihood ratio test in the threshold effect analysis was 0.317 in the adjusted model, which showed that the tendency of the association between 25(OH)D and frailty was monotonical and with no inflexion.

Table 3. Threshold effect analysis of 25(OH)D (nmol/L) using the piece-wise regression model

Variables	Crude [a] OR (95%CI)	Adjusted [b] OR (95%CI)
Continuous	0.967 (0.960, 0.975) ***	0.975 (0.965, 0.984) ***
Cutoff		
≤33.96	0.948 (0.929, 0.967) ***	0.963 (0.939, 0.988) ***
>33.96	0.978 (0.966, 0.989) ***	0.981 (0.966, 0.996) *
p-value of log-likelihood ratio test	0.032	0.317

[a] Crude: no adjustment.

[b] Adjusted for **socio-demographics** (age, gender, marital status, residence, education level, and co-residence), **health characteristics** (smoking, drinking, and regular exercise, hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, and respiratory diseases) and **confounding biomarkers** (CRP, ALB, CHO, CREA, HDLC, LDLC, TG, SOD, MDA, WBC, and HGB).

* <0.05, ** <0.01, *** <0.001.

Subgroup analyses

Subgroup analyses showed the *p*-value for interaction were 0.9753 for gender and 0.1077 for age, which revealed that the association of 25(OH)D level with frailty did not significantly differ by gender and age after adjusted for a series of covariates. (**Figure 2**).

Sensitivity analysis

We performed multivariate analysis in those participants with complete variables and multiple imputations, separately. As displayed in **Supplementary Table S2 (see Additional file 1)**, the present findings showed similar results.

Discussion

In this community-based study, after adjustment for a variety of potential confounding factors, we observed a robust and monotonically negative association of 25(OH)D with frailty among a group of oldest-old population in China. Meanwhile, by examining the relationship between different subgroups of participants, we also proved that this association was consistent across gender and age groups.

Comparison with other studies

The relationship between 25(OH)D level and frailty has rarely been investigated among the oldest-old individuals. As hypothesized, the present findings suggested that 25(OH)D level was related to frailty after adjustment of numerous confounders. The findings from our study were relatively consistent with previous studies involving older adults in the Netherlands(25, 32), Mexico(23), northern Taiwan(33) and German(31).

Limited studies demonstrated the shape of the association between 25(OH)D level and frailty. In the study of 1606 old men aged 73.8 ± 5.9 years in the USA, a segmented negative curvilinear association between 25(OH)D level and odds of frailty was identified(21). However, this association was not observed among 6307 old women in America(20), which was replaced by an U-shaped curvilinear association. For the present study, we identified a robust and monotonically negative association between 25(OH)D and frailty in Chinese older adults.

Chronic diseases, lifestyles, and some biomarkers were studied as potential risk factors of frailty in existing literatures (11, 19, 24). However, the association between 25(OH)D and frailty was not been substantially confounded after adding these covariates in the models of our study. This suggested that 25(OH)D was independently associated with risk of frailty. However, it remains inconclusive that other possible factors, not included in this study, might contribute to the relationship between 25(OH)D and frailty.

Due to differences in latitudes, seasons, measurements of frailty, adequacy of adjustment for potential confounders, and the clinical heterogeneity between races and ethnicities(34), some variations from previous studies were also founded in this study. Firstly, our study reported that the median 25(OH)D level of the elderly was 35.89 nmol/L, which was lower than the median levels of those participants in Taiwan(33), Netherlands(25), and German(27). Besides, the prevalence of frailty was 33.2%, which was much higher compared to 13% in the Japanese elderly(8) and 17% in the USA older women(6). Since the 25(OH)D level and frailty status are closely related to aging(19), these differences could also be partly explained by the oversampling of oldest-old people in this study.

Secondly, the association between 25(OH)D level and frailty has been reported to be different across gender(20, 21, 27, 28, 30). A study of participants in Italy identified that Vitamin D insufficiency was associated with frailty only in men (30). However, conflict results were reported in studies involved older women in the USA(24), Spain(29), and Portugal(28). In this regard, our study detected that 25(OH)D level was associated with frailty regardless of gender, which was similar to the study of individuals in Germany(27). In addition, our study also indicated that this association did not differ between octogenarians', nonagenarians', and centenarians' subgroups.

Strength and limitations

The strength of the current study was a large number of Chinese community-based participants with the collection of plasma blood samples during the survey. It allowed us to investigate the shape of the association between 25(OH)D level and frailty and to adjust for important potential confounding variables. To our knowledge, this was the first study that investigated the relationship between 25(OH)D level and frailty in a nationwide study of Chinese oldest-old people. The present study included a large population of Chinese older adults aged 80 years and over, which allowed robust conclusions to be drawn with respect to these participants.

This study also has certain limitations. First, a dichotomous outcome measure for frailty was used in this study, hence the pre-frail status was not taken into account. Second, some of the clinical diseases were self-reported. For this condition, we adjusted hypertension and diabetes status by clinical data in place of self-reporting so as to eliminate the information bias. Third, this was a descriptive cross-sectional design that did not allow us to evaluate whether change in 25(OH)D level was a cause or a consequence of frailty.

Conclusion

With the population-based design, this study indicates that the 25(OH)D level is monotonically and negatively associated with frailty in the Chinese community-dwelling population. Results of the present study, along with other existing epidemiological studies, reinforce the importance of investigation on the fully explanation of the association between 25(OH)D and frailty. Further longitudinal studies are needed to verify our initial cross-sectional findings, so that we may identify an effective intervention to stem the rapidly increasing prevalence of frailty associated with an aging population.

List Of Abbreviations

CLHLS, Chinese Longitudinal Healthy Longevity Survey; 25-hydroxyvitamin D, 25(OH)D; SOF, Study of Osteoporotic Fractures; FI, Frailty Index; CGA, comprehensive geriatric assessment; CHS, Cardiovascular Health Study; CDC, Center for Disease Control and Prevention; SD, standard variance; IQR, interquartile range; LRT, Likelihood Ratio Test; OR, odds ratio; CI, confidence interval; GAM, generalized additive model; CRP, C reactive protein; ALB, plasma albumin; CHO, total cholesterol; CREA, plasma creatine; SOD, superoxide dismutase; HDLC, high-density lipoprotein cholesterol; LDLC, low-density lipoprotein cholesterol; TG, triglyceride; SOD, superoxide dismutase; MDA, malondialdehyde; WBC, white blood cell count; HGB, hemoglobin.

Declarations

Ethics approval and consent to participate

The CLHLS study was approved by the Research Ethics Committee of Peking University (IRB00001052-13074), and all participants or their proxy respondents provided written informed consent.

Consent for publication

Not applicable.

Availability of data and material

The CLHLS questionnaires are available at https://sites.duke.edu/centerforaging/ programs/chinese-longitudinal-healthy-longevity-survey-clhls/survey-documentation/ questionnaires/. The full datasets used in this analysis are available from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Xiao Qi and Zeng Tieying conceived the study; Xiao Qi and Wu Meiliyang analyze the data; Cui Jinrui, Yuan Mengmei and Chen Ye helped interpret of the data; Xiao Qi wrote the manuscript. All authors contributed to the manuscript revision and approved the final manuscript.

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Figures

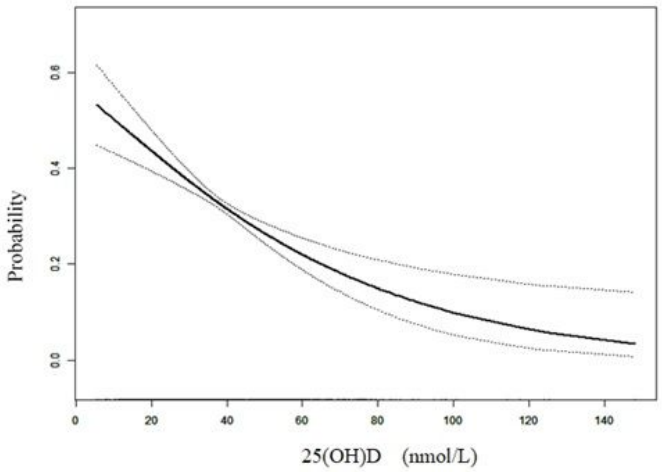

Figure 1. The dose-response relationship of 25(OH)D level and risk of frailty in the full adjusted model. Lines=estimated probability of frailty with 25(OH)D, dotted lines=95% confidence intervals.

Figure 1

The dose-response relationship of 25(OH)D level and risk of frailty adjusted for socio-demographics (age, gender, marital status, residence, education level, and co-residence), health characteristics (smoking, drinking, regular exercise, hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, and respiratory diseases) and confounding biomarkers (CRP, ALB, CHO, CREA, HDLC, LDLC, TG, SOD, MDA, WBC, and HGB). Lines=estimated probability of frailty with 25(OH)D, dotted lines=95% confidence intervals.

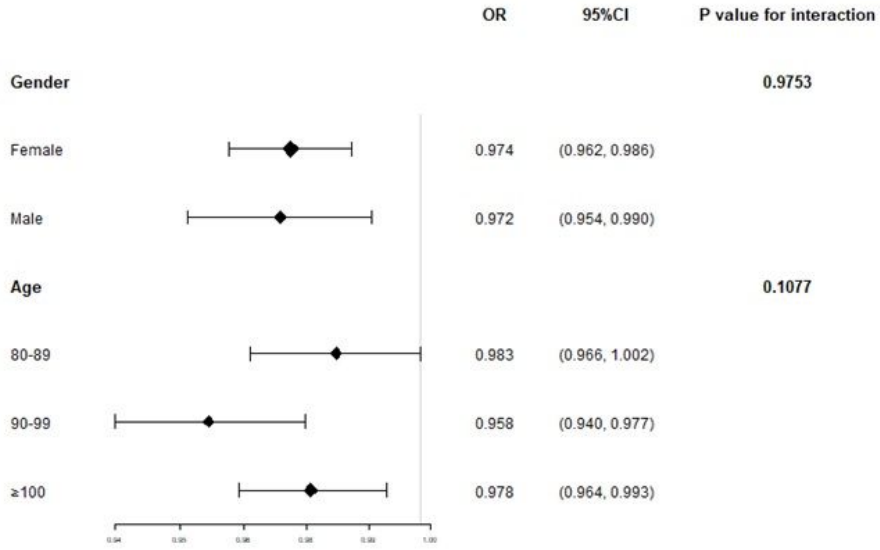

Figure 1. Subgroup analyses for the association between 25(OH)D and frailty in the fully adjusted model.

Figure 2

Subgroup analyses for the association between 25(OH)D and frailty adjusted for marital status, residence, education level, and co-residence, smoking, drinking, and regular exercise, hypertension, diabetes mellitus, heart diseases, cerebrovascular diseases, respiratory diseases, CRP, ALB, CHO, CREA, HDLC, LDLC, TG, SOD, MDA, WBC, and HGB.

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