Serum Albumin and Activities of Daily Living in Chinese Centenarians: A Cross-Sectional Study

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Abstract

Background Objective deterioration in activities of daily living (ADLs) exists among older people, and particularly worsens with age. Considering the criterion standard of positive aging and longevity, little information focusing on centenarians is available. The present study aimed to examine the relationship between serum albumin and ADLs among centenarians in long-lived areas. Methods This population-based cross-sectional study investigated a complete sample of Chinese persons aged ≥100 years in Hainan, the longest-lived area of China (n=1002). We assessed serum albumin levels and basic and instrumental activities of daily living (BADLs and IADLs). Results Of 1002 participants included in the analysis, 287 (28.64%) had BADL disabilities and 648 (64.67%) had IADL disabilities. The median serum albumin level was 38.5 g/L (interquartile range, 36.2–41.3). The multivariable analyses controlling for socio-demographic characteristics, lifestyle, morbidities, and other influential factors showed that albumin level was associated with the total score of BADL (standard β=0.335, P<0.001) and IADL (standard β=0.206, P<0.001). With the increasing of albumin level, the risk of ADLs disability decreased (BADL: odds ratios [OR] = 0.835, 95% Confidence interval [CI]: 0.797-0.876; IADL: OR=0.863, 95%CI: 0.824-0.905). In the stratified analyses, similar results were found in both sex, but were more prominent in women. Conclusions Higher levels of serum albumin was a protective factor for the decline of ADLs in centenarians. This association can be observed in both genders and is more pronounced in women.

Background

Activities of daily living (ADLs) are a core set of essential activities for individuals to live independently and is an important index that determines the quality of life and life expectancy [1]. Physical disability is related to numerous adverse health outcomes such as cognitive decline [2], mental disorder [3], worse resident quality of life [4], and the increased caregiver stress [5, 6]. The population of very old adults aged 85 years and older is increasing at a faster rate than other groups; particularly, the number of centenarians has increased exponentially worldwide [7]. Objective deterioration of functional status exists among centenarians, most of whom depend on help from family or professional aides in their ADLs [6]. An increase in the number of centenarians may indicate a higher proportion of disabilities and poor health in the older population, and eventually increase the burden of medical care and treatment [8].

As an important indicator of protein-energy malnutrition (PEM), hypoalbuminemia is very common among elderly people worldwide. Age increment leads to lower serum albumin (Alb) levels and a higher risk of hypoalbuminemia [9]. Previous studies have shown that hypoalbuminemia is associated with sarcopenia in older adults[10]. Sarcopenia leads to an increased risk of falls and fractures in the elderly, which may eventually contribute to ADL disability. In addition, Alb-related chronic or acute inflammatory conditions may be correlated with the decline of ADLs in the elderly.

Studies have revealed that a strong relationship exists between Alb level and ADL in the general elderly population [9-19]. Given the potentially unique pattern of vulnerability, centenarians deserve more attention. However, only a few studies with a limited sample size have examined its relationship among the oldest old individuals, and contentious findings have been reported in sex difference. Considering the high

prevalence of hypoalbuminemia and functional decline as people age, the relationship between Alb level and ADLs warrants a more focused examination among centenarians.

Therefore, we assessed the distribution characteristics of Alb levels and ADL disability and investigated the association between Alb and ADL impairment especially the sex difference among centenarians using cross-sectional data obtained from a complete sample of a centenarian cohort from Chinese longest-lived areas.

Methods

Study population

We assessed cross-sectional data collected from 2014–2016 in the China Hainan Centenarian Cohort Study (CHCCS) [20], a longitudinal observational study that targeted the population aged 100 years or older in Hainan, China. The CHCCS is based on a complete sample of the Hainan community-dwelling and institutionalized centenarian population conducted by an interdisciplinary research team. The study protocol was approved by the institutional review board of the Chinese People's Liberation Army General Hospital (Beijing, China). All study participants provided written informed consent prior to enrollment.

According to the household register provided by the Civil Affairs Bureau in 2014, there were 1811 living centenarians in total. After a rigorous age validation process, we established contact with 1473 eligible individuals. We also excluded individuals who were not conscious and could not perform ADLs or participate in the questionnaire interview, physical health examination, and blood tests. Finally, 1002 centenarians aged 100–116 years were enrolled during recruitment and baseline data were collected between July 2014 and December 2016.

Activities of daily living

We conducted face-to-face interviews to assess the ability to perform ADL and inspections through relatives or caregivers to ensure effective and reliable investigations. ADLs consist of two components: basic ADLs (BADLs) and instrumental ADLs (IADLs). The Barthel index (BI) and Lawton scale were used to evaluate BADLs and IADLs, respectively.

The BI was developed in 1965 and later modified as a scoring technique that measures the patient's performance in 10 activities of daily life (eating, grooming, bathing, dressing, bowel and bladder care, toilet use, ambulation, transfers, and stair climbing) [21, 22]. Each item is scored 0–5 points, 0–10 points, or 0–15 points according to different evaluation results and summed to a total of 0–100 points. The total BI score is used to classify the individuals' level of dependence as total (0–20), severe (21–60), moderate (61–90), or slight (91–99). A total score of 100 indicates that the patient is independent of assistance from others [23]. In this study, we defined BADL disability as BI $\leq$60 points [24].

The Lawton IADL scale is an appropriate instrument used to assess independent living skills that are considered more complex than the BADLs (using the phone, shopping, preparing food, housekeeping, doing

laundry, using transportation, handling medications, and handling finances) [25, 26]. Each skill measured by the scale requires some degree of both cognitive and physical function [27]. It takes 10–15 minutes to complete with a summary score ranging from 0–8. The total score of the scale sorts IADL dependence into 4 levels: severe (≤2), moderate (3–5), slight (6–7), and none (8). In this study, we defined IADL disability as a Lawton IADL score ≤2.

Serum albumin

Experienced nurses collected 8 ml of blood from each participant in a fasting state using four vacutainer tubes (2 ml each). All blood samples were transported to the clinical laboratory in a chilled transport container (4°C) and assayed within 4 hours. Comprehensive metabolic panel examinations were performed using a fully automatic biochemical autoanalyzer (Cobas 8000; Roche Products Ltd, Basel, Switzerland). Hypoalbuminemia is defined by a serum albumin < 35 g/L [28].

Covariates

For the interview and examination, participants were visited at their residences or nearby clinics by a well-trained interdisciplinary medical group. Using a face-to-face interview in the appropriate regional dialect, the interviewers recorded detailed information on a standardized structured questionnaire. Socio-demographic characteristics assessed included age, gender, education, ethnicity, marital status, educational level, and type of residence. We also considered lifestyle characteristics such as smoking status, alcohol drinking status, and weekly exercise. Standing height and weight were measured using a manufactured instrument, and the body mass index (BMI) was calculated by dividing the body weight by the height (in kg/m^2). Participants with a BMI <18.5 kg/m^2 were categorized as underweight [29]. Respondents were asked to report whether they had been diagnosed and treated by a doctor for any specific medical conditions. The presence of heart disease or stroke was self-reported. The presence of hypertension was defined by a self-report of high blood pressure, and/or sitting systolic blood pressure >140 mmHg and/or diastolic blood pressure >90 mmHg [30]. Similarly, diabetes was defined by self-report and/or a fasting blood glucose concentration of ≥7.0 mmol/L [31]. Impaired renal function was defined by self-report and/or a glomerular filtration rate <60 $ml \cdot min^{-1}/1.73\ m^2$ [32].

Statistical Analysis

The results are presented as medians and interquartile ranges or means ± standard deviations for continuous variables, and as n (%) for categorical variables. Differences among groups were evaluated using the Mann–Whitney *U* test or the chi-squared test, as appropriate. Multivariable linear regression and logistic regression models were constructed to evaluate the associations between Alb and the total score of ADLs. ADL disability (BI ≤60) and IADL disability (Lawton IADL score ≤2) were also used as outcomes and stratified analyses were performed. In the multivariable analyses, we considered socio-demographic characteristics, lifestyles, morbidity, and other influential factors including BMI classification, hemoglobin (Hb), total cholesterol (TC) level, and serum 25-hydroxyvitamin D (25OHD) as covariates. All statistical

analyses were performed using SPSS Statistics version 24.0 (IBM Corporation, Armonk, NY, USA). All tests were two-sided and performed at a 5% significance level.

Results

Baseline characteristics

A total of 1002 centenarians were included in this study, including 822 women, who accounted for 82.04% of the total population. The ages of the participants ranged from 100–116 years, with a median age of 102 years (interquartile range [IQR], 101–104). The participants were mainly of Han ethnicity, illiterate, widowed/divorced/unmarried, and living with their families. The proportions of participants who smoked, drank alcohol, and exercised weekly were all lower than 20%. The median Alb level was 38.5 g/L (IQR, 36.2–41.3) for the entire sample. Participants with hypoalbuminemia had lower levels of Hb, TC, and 25OHD, and a lower prevalence of hypertension (Table 1).

Prevalence of ADL disability

The higher Alb group had a significantly lower rate of BADL and IADL disability than did the lower Alb group (Table 1). The prevalence of BADL disability was 28.64%, and that of IADL disability was 64.67%. Only 19 individuals were completely independent regarding IADL, and accounted for 1.9% of the population.

Results of linear regression models

The standardized total score of BADL and IADL were included in the linear regression models as continuous variable respectively, and socio-demographic characteristics, lifestyle characteristics, morbidities, and other covariates were involved as adjust variables step by step. After adjustment, Alb was found to be significantly associated with ADLs (BADL: standard β=0.335, P<0.001; IADL: standard β=0.206, P<0.001, Table 2). The effect was weakened but in the same direction when the covariates were gradually incorporated. Similar results were found in both women (BADL: standard β=0.347, P<0.001; IADL: standard β=0.205, P<0.001, Table 2) and men (BADL: standard β=0.218, P=0.011; IADL: standard β=0.194, P=0.013, Table 2) but were more prominent in women.

Results of logistic regression models

After adjustment, a significant association existed between Alb level and ADLs disability. The odds ratios (OR) of BADL disability for centenarians with one more g/L Alb was 0.835 (95% Confidence interval [CI]:0.797-0.876), and that of IADL was 0.863 (95%CI: 0.824-0.905). In stratified analyses by sex, the association in women (BADL: OR=0.831, 95%CI: 0.788-0.877; IADL: OR=0.863, 95%CI: 0.819-0.910, Table 3) was stronger than that in men (BADL: OR=0.866, 95%CI: 0.768-0.977; IADL: OR=0.888, 95%CI: 0.795-0.991, Table 3).

Discussion

Prior to our study, only one study had assessed the association between Alb level and ADL among Chinese centenarians [16]. Our data were derived from the 2014–2016 cross-sectional data of the CHCCS, which included a complete sample of a large population in Hainan province. Hainan province has one of the highest life expectancies (76.3 years in 2010) and the highest proportion of centenarians (18.75/100 000) in China [33]. Therefore, our study may have some implications for positive aging and longevity.

As a clinical routinely-tested indicator and modifiable risk-related factor, Alb is important and imperative for providing potential clues for public interventions and long-term clinical care. Among 1002 Hainan centenarians assessed in this study, the average Alb level was 38.5 g/L (IQR, 36.2–41.3). This is lower than that identified in another Chinese longevity cohort with an average age of 97 (IQR, 96–98) years, which showed a mean albumin level of 42.4 ± 4.6 g/L [34]. The difference may be related to the age distribution characteristics of the subjects and differences in laboratory testing. A previous study showed that albumin concentration is related to aging and gradually decreases by 0.08–0.17 g/L per year, with levels tending to decline faster among males than among females [18]. In a study that included 95 Japanese centenarians, the mean Alb concentration was 36.0 ± 4.0 g/L among women and 36.0 ± 5.0 g/L among men [16]. The Alb concentration among centenarians was close to the lower limit of the adult reference value (35.0–50.0 g/L). Even in the high Alb group (with levels >35.0 g/L), a significant proportion of the elderly was ADL disabled. Thus, we have reason to doubt the utility of using this traditional reference in the very old population, which is in line with the findings of Kuzuya et al [35]. There is a need to establish a reference standard for healthy elderly populations, not only of Alb but also other significant serological indicators.

In this study, 287 (28.64%) centenarians were identified as having BADL disability. The prevalence of BADL disability was lower than that reported among older people and centenarians in similar studies regarding the population aged ≥90 years in other countries [36, 37]. Approximately 50% of participants were classified as having BADL disability in the baseline data of a local longevity cohort study, which investigated 433 long-lived individuals aged ≥95 years [34]. In the Chinese Longitudinal Healthy Longevity Survey, a nationwide survey of a randomly-selected half of the counties and cities in 22 of the 31 provinces, covering about 85% of the total population of China, 37.1% of the sample had BADL disability at the baseline [38, 39]. One possible reason for the discrepancy is that diseases or factors of early death are delayed or absent among centenarians. Comparatively, long-lived individuals tend to live in good functional states. Besides, different versions of rating scales with different scoring criteria were used, and different definitions of disability were used among the studies.

BADL functions are essential for an individual’s self-care, whereas IADL functions are more concerned with higher-level skills in specific situations of social living. In our study, only 19 (1.9%) individuals had complete IADL independence according to the total score of the Lawton IADL scale. This means that almost every centenarian had lost at least one aspect of advanced functional independence necessary for daily living. The combination of all IADL items explains a larger portion of the difference in physical and psychological dimensions of quality of life compared to IADL items [40]. The performance of IADL in this sample is worse than that of the younger older population reported in similar studies [40-42]. This may be due to the fact that the incidence rate of ADL disability increases with age [43]. Advanced functions in daily

life are important aspects of mental health and quality of life among older people. Thus, there is a need to pay attention to the impact of such a poor IADL in the very old.

The main finding of our study was that low levels of Alb were associated with ADL disability. Similar results have been reported in previous cross-sectional studies [11, 12, 15] and cohort studies [13, 17]. However, a few studies have reported negative results [44]. Alb plays an essential physiological role in the maintenance of health, including maintaining plasma colloid osmotic pressure and transporting endogenous substances and exogenous drugs. Its correlation with ADL may be attributable to the following hypotheses. As an essential indicator of nutritional status, Alb has great prognostic significance in protein-energy malnutrition. Also, it is a significant marker of acute and chronic inflammatory responses. Both hypoalbuminemia [10], inflammation [45] and malnutrition [46] are associated with reduced muscle mass (sarcopenia) in older adults. The positive association of sarcopenia with falls and fractures in older adults [47] is exact, which would contribute to the decline of ADL. Moreover, Alb plays a vital role in the pathogenesis of organ or system dysfunction/failure [48]. Albumin-associated inflammatory state and the associated poor acute pathological recovery might explain the ADL disability. On the other hand, IADL disability is a multidimensional construct that includes physical and cognitive domains. Significant cognitive decline is typical among older people [49] and is strongly associated with difficulties in IADL [50]. Thus, the severe deterioration of IADL among centenarians is explainable. The mechanism and causal link between Alb and ADL are not precise and need to be assessed in further studies.

Sex difference in this association were controversial in previous research. Our results are similar to the study of Okamura et al., which enrolled 797 men and 1047 women aged 60 to 74 [17]. However, a 3-year follow-up study showed that a combination of low Alb and low cholesterol levels was predictive of reduced functional performance, especially in men [44]. In a study of 97 male extremely longevous individuals (>95 years old) conducted in China, researchers did not observe any association in men. Considering the very advanced level of age, our study recruited a relatively sufficient sample. Therefore, our research may provide some new evidence. However, we still could not determine if the results obtained in the male group are due to this fact or the influence of survivor bias. The crude mortality rate of elderly males is higher than that of females [51]. This may lead to the earlier death of the older men with severe impairment of ADL status and mask the relationship between Alb and impaired ADL. Therefore, more extensive research has to be conducted to understand the relationship entirely.

Several limitations in this study deserve mention. First, due to the cross-sectional design of the study, causal inference is limited. A longitudinal survey will further clarify the clinical significance and predictive effectiveness of Alb in the older population. Second, we excluded some individuals who were unable to participate in interviews and physical examinations before the investigation. The excluded subjects may be more likely in a low level of physical and cognitive function, which may lead to a certain underestimation of the prevalence of ADL disability. Third, the self-reported results of the questionnaire may be biased toward older people with poor cognitive function. Fourth, due to the lack of systematic nutritional assessment, we were unable to verify the exact association between Alb and nutritional status among centenarians.

Conclusions

This study is the first to report on the levels of Alb and prevalence of ADL disability and to explore their association among Chinese centenarians. In this study, the concentration of Alb was low and the prevalences of BADL disability and IADL disability were 28.64% and 64.67%, respectively. Low levels of albumin were associated with a decline in ADL function among centenarians, and this association was gender-specific and more prominent among females. Paying attention to Alb levels among the elderly and properly caring and treating elderly persons with low Alb levels may significantly improve their physical function. However, there is a need to validate whether albumin-deficient interventions are ideal strategies for preventing disability development or improving the independence of older persons through appropriately designed randomized and controlled trials.

Abbreviations

ADL: Activities of daily living; BADL: basic activities of daily living; IADL: instrumental activities of daily living; Alb: Serum albumin; CHCCS: China Hainan Centenarian Cohort Study; BMI: body mass index; Hb: hemoglobin; TC: total cholesterol; 25HOD: serum 25-hydroxyvitamin D; IQR: interquartile range; 95% CI: 95% confidence intervals.

Declarations

Ethics approval and consent to participate

The study obtained ethics approval from the Ethics Committee of the Hainan branch of the Chinese People's Liberation Army General Hospital (No. 301hn11201601). All participants were informed about the study goals and signed informed consent.

Consent for publication

Not applicable.

Availability of data and material

Data can be obtained from the corresponding author upon reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

KH, SSW, and YH conceived and designed the project; KH, SSW, ML, SSY, JHW, WPJ, WZC, and YH collected the data; KH drafted and revised the paper; KH, SSW, WPJ, and WZC conducted the data analysis; ML, SSY, JHW, and YH supervised the analyses and suggested revisions of the paper. ML, SSY, JHW provided administrative, technical, or material support; All the authors have read and approved the final manuscript.

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Tables

Table 1. Prevalence of risk factors for ADL disability at two levels of serum albumin among 1002 centenarians

Characteristics	Total(n=1002)	Serum albumin		P value
		Hypoalbuminemia (n=174)	Normal Alb level (n=828)	
Age, median(IQR),y	102.0(101.0-104.0)	103.0(101.0-105.0)	102.0(101.0-104.0)	0.003
Female,%	822(82.0)	140(80.5)	682(82.4)	0.551
Han ethnicity,%	883(88.1)	156(89.7)	727(87.8)	0.492
Illiterate,%	915(91.3)	162(93.1)	753(91.1)	0.325
Married,%	100(10.0)	16(9.2)	84(10.1)	0.704
Living with families,%	863(86.1)	159(91.4)	704(85.0)	0.027
Current smoker,%	35(3.5)	6(3.5)	29(3.5)	0.963
Current alcohol drinker,%	99(9.9)	14(8.1)	85(10.3)	0.002
Weekly exerciser,%	129(12.9)	11(6.3)	118(14.3)	0.005
BMI<18.5kg/m^2,%	575(57.4)	118(67.8)	457(55.2)	0.005
Alb, median(IQR),g/L	38.5(36.2-41.3)	32.8(30.6-34.2)	39.4(37.7-41.7)	0.001
Hb, median(IQR), g/L	103.0(114.0-123.0)	102.0(94.0-113.0)	116.9(107.0-125.0)	0.001
TC, median(IQR), mmol/L	4.60(4.1-5.3)	4.0(3.4-4.6)	4.66(4.2-5.3)	0.001
25OHD, median(IQR), ng/mL	21.6(16.9-27.8)	20.9(14.0-26.5)	21.6(17.4-28.1)	0.001
Diabetes,%	96(9.6)	18(10.3)	78(9.4)	0.706
Hypertension,%	757(75.6)	121(69.5)	636(76.8)	0.042
Heart disease,%	41(4.1)	5(2.9)	36(4.3)	0.255
Stroke,%	22(2.2)	1(0.6)	21(2.5)	0.153
Renal function	299(29.8)	56(32.2)	243(29.4)	0.457

impaired,%				
BADL disability,%	287(28.6)	94(54.0)	193(23.3)	0.001
IADL disability,%	648(64.7)	151(86.8)	497(60.0)	0.001

Abbreviations: ADL, activities of daily living; IQR, interquartile range; BMI, body mass index; Alb, serum albumin; Hb, hemoglobin; TC, total cholesterol; 25OHD, serum 25-hydroxyvitamin D.

Table 2. Association between serum albumin level and ADLs [a, b]

	BADL			IADL		
	Standard β	Standard error	P	Standard β	Standard error	P
Male						
Crude model	0.241	0.017	0.001	0.292	0.021	0.001
Model 1	0.236	0.018	0.002	0.273	0.020	0.001
Model 2	0.230	0.020	0.006	0.200	0.022	0.009
Model 3	0.218	0.020	0.011	0.194	0.022	0.013
Female						
Crude model	0.405	0.008	0.001	0.272	0.008	0.001
Model 1	0.399	0.008	0.001	0.255	0.008	0.001
Model 2	0.360	0.009	0.001	0.216	0.009	0.001
Model 3	0.347	0.009	0.001	0.205	0.009	0.001
Total						
Crude model	0.373	0.007	0.001	0.271	0.008	0.001
Model 1	0.369	0.007	0.001	0.256	0.007	0.001
Model 2	0.344	0.008	0.001	0.213	0.008	0.001
Model 3	0.335	0.008	0.001		0.206	0.008	0.001

[a] Crude model: None adjusted;

Model 1：Adjusted for age, ethnicity, marriage, educational levels, residence type

Model 2：Model 1 plus smoking status, alcohol drinking status, weekly exercise, BMI classification, hemoglobin, total cholesterol, serum 25-hydroxyvitamin D

Model 3：Model 2 plus diabetes, hypertension, heart disease, stroke, renal function impaired.

[b] ADLs were transformed to Z score with a mean of 0 and standard deviation (SD) of 1.

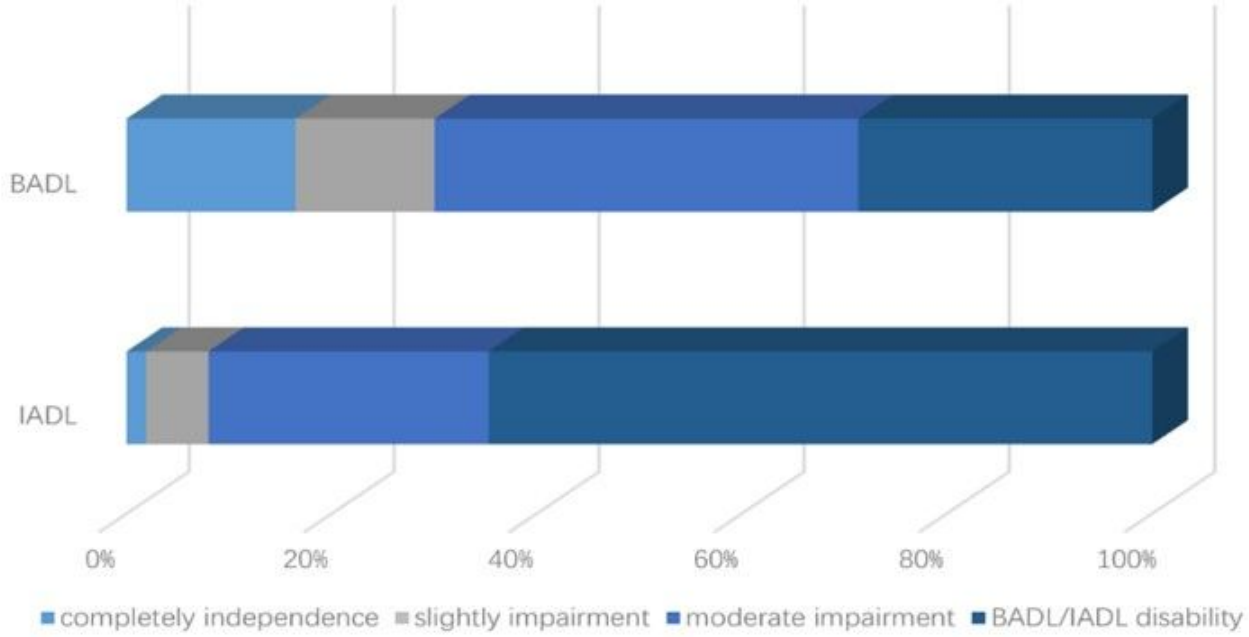
Table 3. Association between serum albumin level and BADL/IADL disability [a, b]

	Total	Male	Female
BADL disability			
Crude model	0.829(0.798,0.862)	0.899(0.824,0.982)	0.813(0.778,0.850)
Model 1	0.829(0.797,0.862)	0.889(0.809,0.977)	0.814(0.779,0.851)
Model 2	0.832(0.794,0.872)	0.864(0.767,0.973)	0.827(0.785,0.871)
Model 3	0.835(0.797,0.876)	0.866(0.768,0.977)	0.831(0.788,0.877)
IADL disability			
Crude model	0.858(0.826,0.892)	0.857(0.788,0.932)	0.854(0.818,0.892)
Model 1	0.856(0.823,0.891)	0.861(0.789,0.939)	0.855(0.818,0.894)
Model 2	0.861(0.822,0.903)	0.883(0.793,0.983)	0.859(0.815,0.905)
Model 3	0.863(0.824,0.905)	0.888(0.795,0.991)	0.863(0.819,0.910)

[a] The adjusted covariates in models are the same as in Table 2.

[b] Described as OR (95%CI).

Figures



The distribution of BADL is different from that of IADL by chi-square test. (P<0.001)

Figure 1

ADL distribution according to the score of the Barthel index and Lawton Scale. The distribution of BADL is different from that of IADL by chi-square test. (P<0.001)

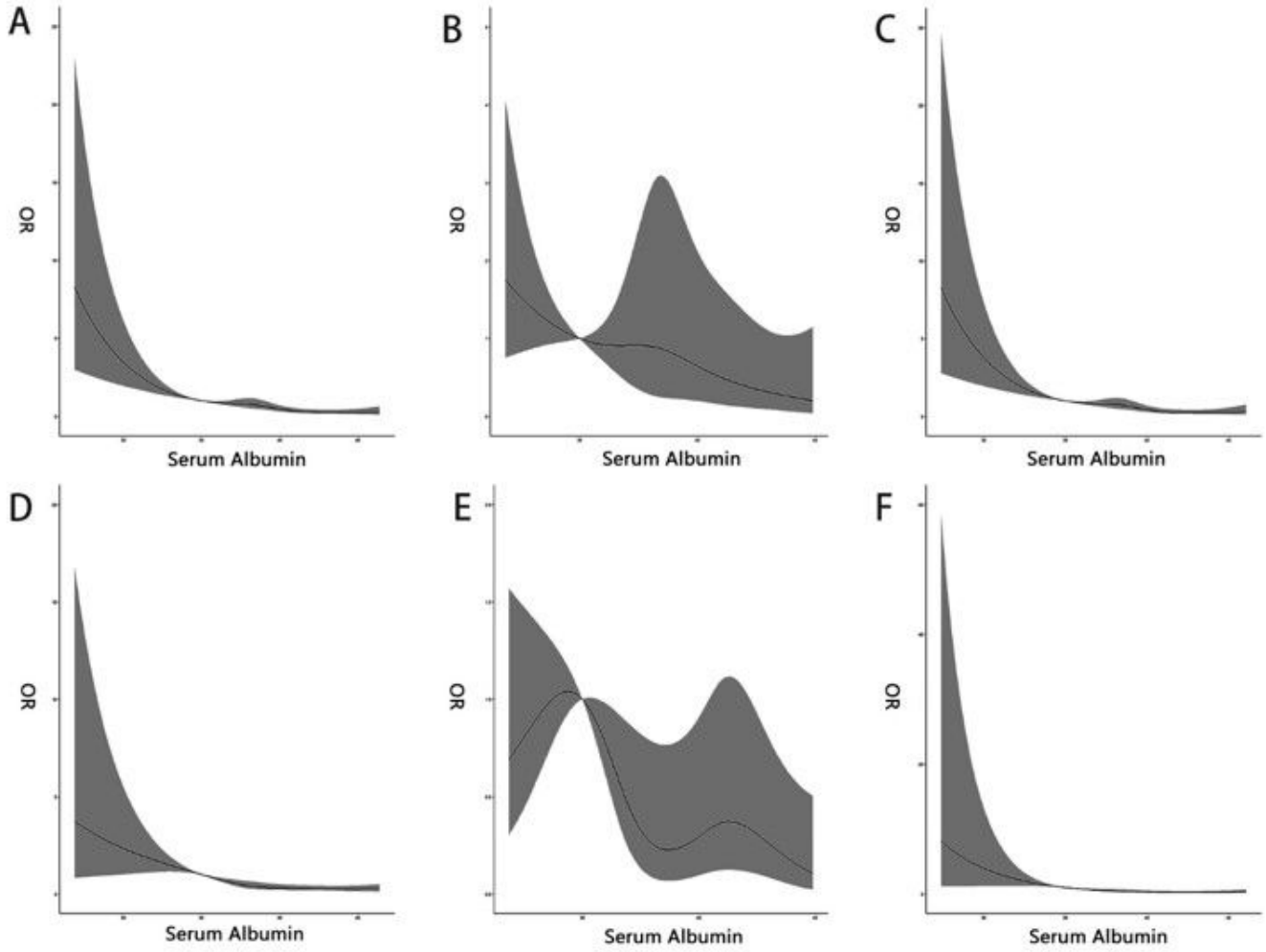


Figure 2

Restricted cubic splines of the relationship between serum albumin and the risk of ADL disability. The y-axis represents the odds ratio, and the x-axis is serum albumin concentration. The solid line shows the odds ratio estimate and the shaded part the 95% confidence intervals. All adjusted for age, ethnicity, marriage, educational levels, residence type, smoking status, alcohol drinking status, weekly exercise, BMI classification, hemoglobin, total cholesterol, serum 25-hydroxyvitamin D and hypertension. A: total BADL disability; B: male BADL disability; C: female BADL disability; D: total IADL disability; E: male IADL disability; F: female IADL disability (P for nonlinear relationship =0.025).