Malnutrition is positively associated with cognitive decline in centenarians and oldest-old adults: A cross-sectional study

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Summary

Background Cognitive decline is a growing public health concern. However, presently, only a few large-scale studies are available on the prevalence of cognitive decline worldwide, and the relationship between nutrition and cognitive decline remains unclear and requires further investigation, especially among Chinese centenarians and oldest-old adults. This study aimed to assess the prevalence of cognitive decline among Chinese centenarians and oldest-old adults, its associated factors, and explore a possible connection with nutrition, to provide new directions for the prevention of cognitive decline in Chinese centenarians and oldest-old adults.

Methods Based on the China Hainan Centenarian Cohort Study (CHCCS), a household survey was conducted among all the centenarians and oldest-old adults residing in 16 cities and counties of Hainan province from June 2014 to June 2016. This study included 946 centenarians and oldest-old adults (412 and 534, respectively). Cognitive function was measured using the mini-mental state examination (MMSE).

Findings The total prevalence of cognitive decline was 76·6% (725 participants). Centenarians had a significantly higher prevalence of cognitive decline compared to oldest-old adults [359 centenarians (87·1%) vs. 366 oldest-old adults (68·5%)]. Centenarians and oldest-old adults with cognitive decline had significantly lower prognostic nutritional index (PNI) and mini nutrition assessment-short form (MNA-SF) than those without cognitive decline ($P < 0·05$). Multivariate logistic regression analyses showed that participants with higher PNI and MNA-SF were less likely to have cognitive decline. Multivariate linear regression analyses showed that PNI and MNA-SF were positively associated with MMSE ($P < 0·05$).

Interpretation Malnutrition was positively associated with cognitive decline among Chinese centenarians and oldest-old adults. It is therefore important for clinicians and community health workers to pay attention to malnutrition in these populations and provide supplemental nutrients to prevent cognitive decline.

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Keywords: Cognitive decline; Centenarians; Malnutrition; Oldest-old adults

Introduction

With the population of older adults steadily increasing, the prevalence of cognitive decline, a gradual process of transition in cognitive capacity with increasing age, is also increasing.[1] Age, gender, education level and genetic susceptibility are well-known risk factors for cognitive decline,[2] and its prevalence increases exponentially from the age of 65.[3] In 2015, 8·5% of the global population (617 million) were aged over 65 years, and this rate is expected to rise to 12% (1 billion) by 2030, and 16·7% (1·6 billion) by 2050.[4] Furthermore, there are nearly 10 million new cases of cognitive decline every year, and this number is expected to triple by 2050. Approximately, this disease affects 50 million people worldwide and incurs 2 trillion in healthcare costs per year. Cognitive decline is the main cause of disability and dependence among older adults, and the high social and economic burden caused by this disease makes it a public health concern.[5] Additionally, cognitive decline raises the risk of many age-related diseases, as described previously in the literature.[6]

While ageing is the strongest factor associated with cognitive decline, other factors like malnutrition might be involved.[7] Malnutrition refers to the lack of energy and other nutrients usually due to inadequate diet, poor absorption and excessive loss of nutrients, and it has adverse effects on health. A previous study showed that 8·4% of older adults were malnourished, and 42·7% were at risk of malnutrition.[8] The Singapore Longitudinal Ageing Studies also indicated that the prevalence of malnutrition was 42%, and its prevalence among the cognitive decline was 63%.[9] The prevalence of malnutrition has been found to be high among the elderly, and directly related to cognitive decline.[10–14] Nutritional status might play an important role in the management and prevention of cognitive decline.[15] However, presently, there is a lack of large-scale research on the prevalence of cognitive decline worldwide, including Europe and USA, and the relationship between nutrition and cognitive decline remains unclear and requires further investigation, especially among Chinese centenarians and oldest-old adults. Therefore, this study aimed to assess the prevalence of cognitive decline and its associated factors. Furthermore, we planned to determine whether there is a relationship between cognitive decline and nutrition, to provide new directions for preventing cognitive decline in Chinese centenarians and oldest-old adults.

Research in context

Evidence before this study

We searched MEDLINE, Embase, and the Cochrane Database of Systematic Reviews from 2001 to 2020. Search terms included Aged, 80 and over, Centenarians, Cognitive Dysfunction, and Malnutritionm [MeSH Terms]. We observed that the prevalence of malnutrition has been reported to rise among the elderly and found to be directly related to cognitive decline. However, presently, few studies has focused on the relationship between nutrition and cognitive decline among Chinese centenarians and oldest-old adults.

Added value of this study

We found malnutrition positively associated with cognitive decline among Chinese centenarians and oldest-old adults, and supported avoiding the development of malnutrition as a strategy for preventing cognitive decline.

Implications of all the available evidence

It is important for clinicians and community health workers to pay attention to malnutrition in the elderly, and provide supplemental nutrients to prevent cognitive decline.

Methods

Based on the China Hainan Centenarian Cohort Study (CHCCS), a household survey was conducted among all the centenarians and oldest-old adults residing in 16 cities and counties of Hainan province from June 2014 to June 2016 based on a demographics list provided by the Department of Civil Affairs in Hainan province, China.[16] A survey sample of 1863 cases included 966 centenarians and 897 oldest-old adults aged 80–99 years.

Inclusion criteria: (1) aged ≥80 years; (2) residing in Hainan province. Exclusion criteria: (1) presence of neurodegenerative diseases including Alzheimer's disease and vascular dementia (1%; 10 centenarians and 2 oldest-old adults); (2) incomplete mini-mental state examination (MMSE) and missing data (nonresponse rate: 49%; 544 centenarians and 361 oldest-old adults). Alzheimer's disease was diagnosed by chief physicians based on medical history, symptoms of memory loss, language impairment, personality change and cognitive decline, and cerebral imaging.[17] Vascular dementia referred to dementia caused by cerebrovascular disease.[18] Finally, this study included 412 centenarians and 534 oldest-old adults (Figure 1). This study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of Chinese PLA General Hospital (301hn11-206-01). All participants or their legal guardians provided written informed consent before participation.

The household survey method was used to collect basic information with interview questionnaires. Physical examinations and blood tests were conducted by trained doctors and nurses who could communicate in the local language. Variables assessed in this study included age, gender, body mass index (BMI), education level (i.e., illiteracy, elementary school level and junior high school level), living situation (alone or not), work type (mental or manual labour), smoking, drinking, hypertension, diabetes, coronary artery disease (CAD), anaemia, white blood cells, neutrophils, lymphocytes, albumin, C-reactive protein, red blood cell distribution width (RDW), mean corpuscular volume (MCV), mean corpuscular haemoglobin concentration (MCHC), blood glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), prognostic nutritional index (PNI) and mini nutrition assessment-short form (MNA-SF). Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of antihypertensive drug.[19] Diabetes was defined as fasting blood glucose ≥7·0 mmol/L, or the use of antidiabetic drug/insulin.[20] CAD was defined by chief physicians based on medical history, symptoms of typical angina, cardiac markers and tests, such as electrocardiogram, echocardiogram, computed tomography, and coronary arteriography, according to the American College of Cardiology/American Heart Association/European Society of Cardiology guidelines.[21–23] Anaemia was defined if haemoglobin level was lower than 120 g/L in males or 110 g/L in females.[24] PNI is a nutritional screening tool, calculated as follows: serum albumin (g/L) + 0·005 × total lymphocyte count (10^9/L).[25]

The core observation index was MMSE, as its association with cognitive function has been established;[26] the Georgia Centenarian Study confirmed that age and education could significantly affect MMSE. The Chinese version of the MMSE has been validated in several previous studies.[27] Cognitive decline was defined when older adults had reduced MMSE after excluding neurodegenerative diseases such as Alzheimer's disease and vascular dementia. The cut-off points for cognitive decline differed with respect to the level of education: illiteracy at 17 points, elementary school level at 20 points, and junior high school level at 24 points.[28]

Statistical analyses

Quantitative data with normal distribution are described descriptively with mean ± standard deviation, and their differences were compared using the independent sample *t*-test. Quantitative data with skewed distribution are described with median (interquartile range), and their differences were compared using the Mann–Whitney U test. Distribution was determined using Kolmogorov–Smirnov and

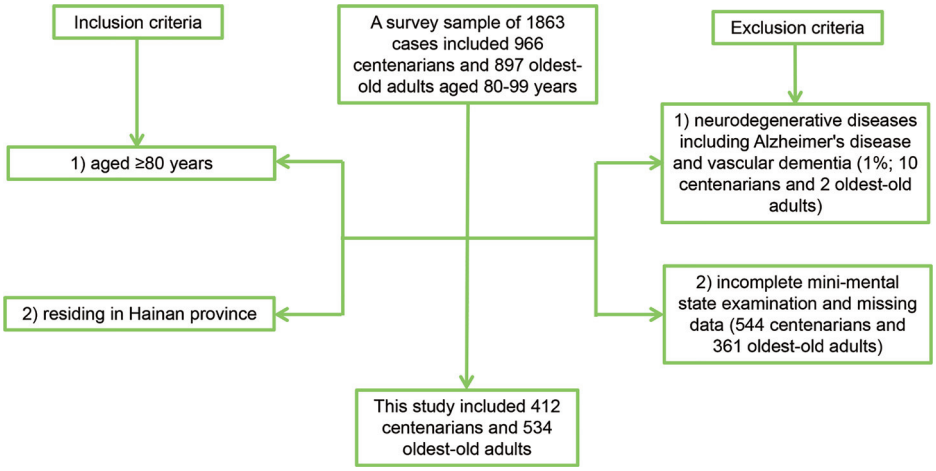

Figure 1. The numbers of cases included and excluded in this study.

Shapiro–Wilk tests. Categorical data are described as number (percentage), and their differences were compared using Chi-square test. Receiver operator characteristic (ROC) curve and area under the curve (AUC) were used to analyse the efficacy of PNI or MNA-SF in identifying all participants without cognitive decline. Multivariate logistic regression analysis was performed with cognitive decline as the dependent variable, and with PNI (MNA-SF), age, being female, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT, and AST as the independent variables. Multivariate linear regression analysis was performed with MMSE as the dependent variable, and with PNI (MNA-SF), age, being female, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT, and AST as independent variables. Another multivariate logistic regression analysis was performed with oldest-old adults/centenarians as the dependent variable, and with being female, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, white blood cell, neutrophil, C-reactive protein, RDW,

Characteristics	With cognitive decline (*n* = 725)	Without cognitive decline (*n* = 221)	*P*
Age (year)	99(85,102)	85(81,96)	<0·001
Gender, *n* (%)			<0·001
Males	184(25·4)	110(49·8)	
Females	541(74·6)	111(50·2)	
BMI (kg/m^2)	19(17,22)	20(18,23)	<0·001
BMI <18.5 kg/m^2	300(41·4)	60(27·1)	<0·001
BMI 18.5 kg/m^2 to 24 kg/m^2	337(46·5)	111(50·2)	
BMI ≥24 kg/m^2	88(12·1)	50(22·6)	
Education degree, *n* (%)			<0·001
Illiteracy	624(86·1)	149(67·4)	
Elementary school level	75(10·3)	47(21·3)	
Junior high school level	26(3·6)	25(11·3)	
Living alone, *n* (%)	114(15·7)	46(20·8)	0·077
Mental labour, *n* (%)	710(97·9)	206(93·2)	<0·001
Smoking, *n* (%)	68(9·4)	39(17·6)	0·001
Drinking, *n* (%)	92(12·7)	40(18·1)	0·042
Hypertension, *n* (%)	523(72·1)	160(72·4)	0·940
Diabetes, *n* (%)	73(10·1)	22(10·0)	0·961
CAD, *n* (%)	37(5·1)	19(8·6)	0·054
Anaemia, *n* (%)	502(73·4)	223(81·5)	<0·001
White blood cells (10^9/L)	5·96(5·02,7·10)	6·22(5·26,7·53)	0·027
Neutrophils (10^9/L)	0·55(0·49,0·62)	0·57(0·48,0·64)	0·281
Lymphocytes (10^9/L)	0·31(0·25,0·38)	0·31(0·24,0·37)	0·278
Albumin (g/L)	40·7(37·8,42·9)	42·6(40·0,44·7)	<0·001
C-reactive protein (mg/dL)	0·15(0·06,0·37)	0·14(0·07,0·33)	0·590
RDW (%)	14·1(13·3,15·2)	13·8(13·1,14·7)	<0·001
MCV (fl)	92·8(87·4,96·5)	93·8(89·4,97·0)	0·016
MCHC (g/L)	314·0(305·0,320·5)	317·0(309·0,324·0)	<0·001
Blood glucose (mmol/L)	4·68(4·05,5·50)	4·38(3·87,5·15)	0·005
ALT (U/L)	10·8(8·4,14·5)	12·2(9·9,15·8)	<0·001
AST (U/L)	21·5(18·6,25·7)	21·7(19·0,26·1)	0·421
MMSE	10(6,13)	23(20,26)	<0·001
PNI	40·7(37·8,42·9)	42·6(40·0,44·7)	<0·001
MNA-SF	9(8,10)	10(9,11)	<0·001

***Table 1*: Characteristics of centenarians and oldest-old adults with and without cognitive decline.**
Abbreviations: BMI: body mass index; CAD: cardiovascular diseases; RDW: red blood cell distribution width; MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALT: alanine aminotransferase; AST: aspartate aminotransferase; MMSE: mini-mental state examination; PNI: prognostic nutritional index; MNA-SF: mini nutrition assessment-short form.

MCV, MCHC, blood glucose, ALT, AST, PNI (MNA-SF), and MMSE as independent variables. A p level of 0·05 was considered significant. Statistical analyses were performed using SPSS version 19·0 (IBM Corp; Armonk, NY).

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Results

Univariate analyses

among 946 cases over 80 years old, the total prevalence of cognitive decline was 76·6% (359 centenarians and 366 oldest-old adults). Characteristics of all participants are shown in Table 1; centenarians (412 cases) and oldest-old adults (534 cases) with and without cognitive decline are shown in supplementary Table 1 and supplementary Table 2, respectively. PNI and MNA-SF were significantly lower in the cases with cognitive decline than those without cognitive decline for all participants ($P < 0·05$). PNI was negatively associated with cognitive decline in univariate logistic regression analysis ($P < 0·001$; Odds ratio: 0.86; 95CI: 0.83−0.90) and positively associated with MMSE in univariate linear regression analysis ($P < 0·001$; B: 0.60; 95CI: 0.50−0.71) in centenarians and oldest-old adults. MNA-SF was negatively associated with cognitive decline in univariate logistic regression analysis ($P < 0·001$; Odds ratio: 0.75; 95CI: 0.68−0.82) and positively associated with MMSE in univariate linear regression analysis

Characteristics	Cognitive decline[a]			MMSE[b]		
	Odds ratio	95% CI	*P*	*B*	95% CI	*P*
PNI	0·94	0·89−0·99	0·017	0·33	0·20−0·45	<0·001
Age	1·05	1·02−1·07	<0·001	-0·18	-0·23−0·13	<0·001
Females	2·08	1·40−3·10	<0·001	-3·31	-4·32−2·30	<0·001
BMI <18.5 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	1·15	0·67−1·98	0·613	-0·08	-0·98−0·83	0·870
BMI ≥24 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	1·17	0·73−1·88	0·508	0·02	-1·19−1·24	0·971
Living alone	0·77	0·50−1·16	0·212	1·01	-0·04−2·05	0·059
Mental labour	1·31	0·57−3·05	0·527	-1·93	-4·23−0·38	0·101
Smoking	0·83	0·50−1·39	0·476	-0·50	-1·85−0·86	0·472
Drinking	0·89	0·55−1·41	0·609	-0·36	-1·53−0·80	0·542
Hypertension	1·05	0·71−1·55	0·819	-0·68	-1·59−0·24	0·147
Diabetes	0·62	0·31−1·23	0·620	1·36	-0·28−2·99	0·103
CAD	0·80	0·42−1·51	0·483	0·68	-0·99−2·35	0·426
Anaemia	0·99	0·62−1·60	0·972	0·15	-0·88−1·19	0·772
White blood cells	0·91	0·82−1·01	0·070	0·14	-0·11−0·38	0·274
Neutrophils	0·97	0·36−2·59	0·950	-0·05	-2·02−1·93	0·963
C-reactive protein	1·02	0·85−1·22	0·846	-0·09	-0·50−0·33	0·687
RDW	1·19	1·02−1·40	0·029	-0·26	-0·55−0·04	0·086
MCV	1·01	0·99−1·04	0·312	-0·02	-0·08−0·03	0·406
MCHC	0·99	0·97−1·01	0·154	0·03	0·00−0·07	0·042
Blood glucose	1·20	1·05−1·37	0·007	-0·34	-0·59−0·08	0·009
ALT	0·99	0·96−1·02	0·325	0·03	-0·05−0·10	0·508
AST	1·01	0·98−1·04	0·557	0·00	-0·07−0·07	0·911

***Table 2*: Multivariate analysis of PNI with cognitive decline or MMSE in centenarians and oldest-old adults.**

Abbreviations: PNI: prognostic nutritional index; MMSE: mini-mental state examination; CI: confidence interval; BMI: body mass index; CAD: cardiovascular diseases; RDW: red blood cell distribution width; MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALT: Alanine aminotransferase; AST: aspartate aminotransferase.

Notes:

[a] Multivariate Logistic regression analysis was used to performed with cognitive decline as the dependent variables, and with PNI, age, being female, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

[b] Multivariate Linear regression analysis was used to performed with MMSE as the dependent variables, and with PNI, age, females, BMI, living alone, mental labour, smokers, drinkers, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

($P < 0{\cdot}001$; B: 1.11; 95CI: 0.90–1.33) in centenarians and oldest-old adults.

Multivariate analyses

Multivariate logistic regression analyses showed that participants with higher PNI and MNA-SF were less likely to have cognitive decline (Tables 2–4 and Supplementary Table 3). Multivariate linear regression analyses showed that PNI and MNA-SF were positively associated with MMSE ($P < 0{\cdot}05$ Tables 2–4; and Supplementary Table 3). PNI was negatively associated with cognitive decline in multivariate logistic regression analysis ($P = 0{\cdot}017$; Odds ratio: 0.94; 95CI: 0.89–0.99) and positively associated with MMSE in multivariate linear regression analysis ($P < 0{\cdot}001$; B: 0.33; 95CI: 0.20 −0.45) in centenarians and oldest-old adults. MNA-SF was negatively associated with cognitive decline in multivariate logistic regression analysis ($P = 0{\cdot}042$; Odds ratio: 0.86; 95CI: 0.75–1.00) and positively associated with MMSE in multivariate linear regression analysis ($P = 0{\cdot}001$; B: 0.51; 95CI: 0.22–0.81) in centenarians and oldest-old adults.

ROC curves

PNI and MNA-SF could identify all participants without cognitive decline. As shown in the ROC curve in Figure 2a, the AUC for PNI to identify all participants without cognitive decline was 0·652 (0·611–0·692; $P < 0{\cdot}001$), and the cut-off point was 41·9, with a sensitivity of 0·602 and specificity of 0·655. The AUC of MNA-SF to identify all participants without cognitive decline was 0·654 (0·614–0·694; $P < 0{\cdot}001$) (Figure 2b), and the cut-off point was 9·5 with sensitivity of 0·615 and specificity of 0·600.

Characteristics	Cognitive decline[a]			MMSE[b]		
	Odds ratio	95% CI	*P*	*B*	95% CI	*P*
PNI	0·93	0·84–1·03	0·186	0·32	0·15–0·50	<0·001
Age	1·03	0·92–1·16	0·584	-0·12	-0·31–0·07	0·222
Females	5·26	2·34–11·86	<0·001	-4·22	-5·91–2·53	<0·001
BMI <18.5 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	0·67	0·16–2·84	0·583	-0·03	-1·25–1·20	0·967
BMI ≥24 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	0·56	0·13–2·35	0·426	-1·54	-4·10–1·02	0·237
Living alone	0·59	0·27–1·31	0·197	1·41	-0·22–3·04	0·089
Mental labour	2·97	0·36–24·33	0·311	-5·75	-10·99–0·51	0·032
Smoking	3·22	0·93–11·18	0·065	-3·03	-5·29–0·76	0·009
Drinking	1·38	0·52–3·69	0·519	-1·15	-2·92–0·62	0·201
Hypertension	1·56	0·73–3·33	0·256	-0·78	-2·15–0·59	0·264
Diabetes	0·30	0·07–1·36	0·304	2·12	-0·62–4·86	0·129
CAD	0·65	0·16–2·68	0·554	0·52	-2·53–3·57	0·737
Anaemia	2·24	1·03–4·88	0·043	-0·34	-1·63–0·94	0·600
White blood cells	1·02	0·84–1·24	0·832	0·05	-0·29–0·39	0·774
Neutrophils	0·09	0·21–4·66	0·987	-0·50	-2·52–1·53	0·631
C–reactive protein	0·80	0·54–1·19	0·275	0·41	-0·38–1·20	0·307
RDW	1·17	0·84–1·50	0·420	0·02	-0·44–0·48	0·938
MCV	1·02	0·97–1·07	0·420	-0·03	-0·10–0·05	0·518
MCHC	1·00	0·98–1·03	0·889	0·04	-0·01–0·08	0·099
Blood glucose	1·32	0·95–1·85	0·103	-0·27	-0·85–0·31	0·354
ALT	0·99	0·94–1·03	0·530	-0·01	-0·12–0·10	0·798
AST	0·99	0·95–1·03	0·661	0·04	-0·05–0·13	0·408

***Table 3*: Multivariate analysis of PNI with cognitive decline or MMSE in centenarians.**

Abbreviations: PNI: prognostic nutritional index; MMSE: mini-mental state examination; CI: confidence interval; BMI: body mass index; CAD: cardiovascular diseases; RDW: red blood cell distribution width;MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Notes:

[a] Multivariate Logistic regression analysis was used to performed with cognitive decline as the dependent variables, and with PNI, age, females, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

[b] Multivariate Linear regression analysis was used to performed with MMSE as the dependent variables, and with PNI, age, females, BMI, living alone, mental labour, smokers, drinkers, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

Characteristics	Cognitive decline[a]			MMSE[b]		
	Odds ratio	95% CI	*P*	*B*	95% CI	*P*
PNI	0·93	0·87–0·99	0·028	0·37	0·19–0·55	<0·001
Age	1·11	1·05–1·17	<0·001	-0·26	-0·38–0·14	<0·001
Females	1·59	0·98–2·56	0·059	-2·95	-4·26–1·64	<0·001
BMI <18.5 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	1·20	0·62–2·33	0·588	0·21	-1·57–1·15	0·759
BMI ≥24 kg/m^2/ 18.5 kg/m^2 to 24 kg/m^2	1·30	0·77–2·21	1·302	0·39	-1·09–1·86	0·607
Living alone	0·89	0·54–1·49	0·668	0·71	-0·69–2·11	0·318
Mental labour	1·09	0·42–2·80	0·865	-0·55	-3·25–2·14	0·686
Smoking	0·53	0·29–0·98	0·044	0·91	-0·83–2·65	0·304
Drinking	0·78	0·44–1·37	0·384	0·07	-1·63–1·50	0·934
Hypertension	1·00	0·62–1·61	0·992	-0·84	-2·11–0·43	0·195
Diabetes	0·68	0·29–1·59	0·370	0·74	-1·44–2·93	0·504
CAD	0·93	0·44–1·99	0·858	0·46	-1·60–2·51	0·664
Anaemia	0·63	0·32–1·22	0·172	0·81	-0·90–2·52	0·354
White blood cells	0·88	0·77–1·00	0·056	0·12	-0·23–0·48	0·498
Neutrophils	0·84	0·09–7·37	0·878	3·68	-2·12–9·48	0·213
C–reactive protein	1·12	0·88–1·43	0·355	-0·26	-0·77–0·25	0·318
RDW	1·18	0·98–1·43	0·085	-0·39	-0·79–0·01	0·054
MCV	1·01	0·98–1·04	0·552	-0·02	-0·10–0·05	0·539
MCHC	0·98	0·96–1·00	0·080	0·04	-0·01–0·10	0·119
Blood glucose	1·24	1·06–1·46	0·008	-0·37	-0·66–0·08	0·013
ALT	0·98	0·94–1·03	0·464	0·05	-0·07–0·17	0·376
AST	1·02	0·97–1·06	0·482	-0·02	-0·13–0·10	0·794

***Table 4*: Multivariate analysis of PNI with cognitive decline or MMSE in oldest-old adults.**

Abbreviations: PNI: prognostic nutritional index; MMSE: mini-mental state examination; CI: confidence interval; BMI: body mass index; CAD: cardiovascular diseases; RDW: red blood cell distribution width;MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Notes:

[a] Multivariate Logistic regression analysis was used to performed with cognitive decline as the dependent variables, and with PNI, age, females, BMI, living alone, mental labour, smoking, drinking, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

[b] Multivariate Linear regression analysis was used to performed with MMSE as the dependent variables, and with PNI, age, females, BMI, living alone, mental labour, smokers, drinkers, hypertension, diabetes, CAD, anaemia, white blood cell, neutrophil, C-reactive protein, RDW, MCV, MCHC, blood glucose, ALT and AST as the independent variables.

Centenarians/oldest-old adults

Centenarians had a significantly higher prevalence of cognitive decline than oldest-old adults (87·1% vs. 68·5%, $P < 0·001$). Characteristics of 412 centenarians and 534 oldest-old adults among 946 cases over 80 years old were shown in Table 5. MMSE, PNI and MNA-SF were significantly lower among the centenarians than oldest-old adults ($P < 0·05$). Multivariate logistic analyses showed that centenarians were more likely to have lower MMSE, PNI and MNA-SF ($P < 0·05$; Supplementary Table 4).

Discussion

The most significant independent risk factor for cognitive decline is age, but other contributing factors include demographic, genetic, and nutritional parameters.[29] Ongoing population ageing will lead to a doubling of the number of people aged over 65 years in the coming five decades. There is evidence that malnutrition is a widespread problem among the ageing population;[30] in fact, hypoalbuminemia is related to mortality in the elderly, whether they live in a community, in a hospital, or are institutionalised.[31] Albumin is a good marker of nutritional status in clinically stable people, and PNI is a nutritional screening tool calculated using albumin level and lymphocyte count.[32] This study found that PNI and MNA-SF were significantly lower in the centenarians and in those with cognitive decline than others, and had significantly positive association with MMSE.

Older adults are at risk of malnutrition, a major public health problem in tropical and subtropical regions of the world, and it usually occurs during a period of energy deficiency due to poor socio-economic and environmental conditions.[33] Nutritional status impacts health and cognitive function, and malnutrition could lead to cognitive decline in the elderly.[34] This study identified malnutrition as a significant factor for cognitive decline, and other studies have found that energy deficiency could lead to nerve cell damage, central

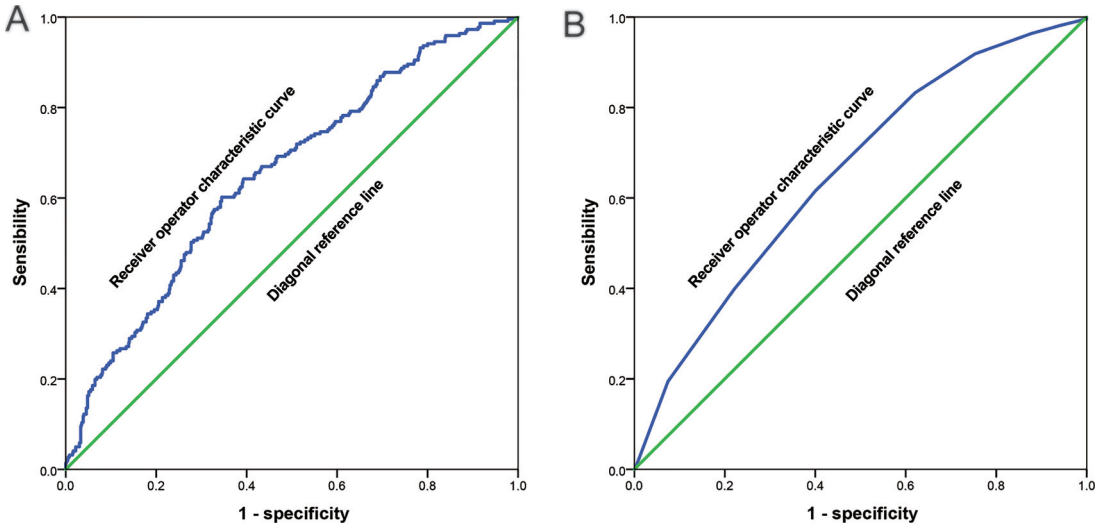

Figure 2. (a) The receiver operator characteristic curve of prognostic nutritional index to identify all participants without cognitive decline; and (b) The receiver operator characteristic curve of mini nutrition assessment-short form to identify all participants without cognitive decline.

nervous system (CNS) deregulation, and negative cognitive outcomes.[35] Malnutrition is marked by insufficient protein and nutrient intake and results in energy deficiency in neurons, promoting the development of neurological disorders.[36] In the ageing population, such physiological changes further accelerate the ageing process and increase the vulnerability of neurons to damage. Therefore, in older adults, malnutrition could be a significant risk factor for cognitive decline during the ageing process.

Cognitive decline might be influenced by nutritional status. Nutritional problems have been found to be related to adverse consequences, such as a decline in cognitive ability.[37] Sugita et al. have realized that nutritional index, especially PNI, is significantly correlated with cognitive function.[38] Kimura et al. have suggested that patients with cognitive decline had lower MNA-SF and higher prevalence of malnutrition than normal people.[39] Malnutrition has been identified to be associated with cognitive function in the elderly. In the Georgia Centenarian Study designed to test the correlates of healthy longevity, the role of nutrition was focused on regarding the change in cognitive function.[40]

Change in the pathophysiology of cognitive decline in the oldest-old adults has many complex and heterogeneous causes. Malnutrition is a potential mechanism of cognitive decline, which might be related to the decrease of energy intake caused by the increase of metabolic disorders and energy consumption. Nutritional status might affect cognition and mood through the following pathways. As in the overeating and obesity, malnutrition could generate inflammatory responses in peripheral and central immune cells, and affect blood-brain interface and circulating factors regulating cognitive function. Neuroprotective foods might provide a means to protect the aging brain from such damage by reducing brain inflammation and oxidative stress, thereby preventing cognitive decline in the elderly.[41] Oxidative stress and inflammatory responses are etiological factors for the development of insulin resistance, cardiometabolic diseases, and cognitive decline.[42] As a key reaction operating interdependently during the ageing process, insulin resistance significantly diminishes the responsiveness of peripheral tissues and affects nutritional metabolism and status.[43]

Previous studies have found that Mediterranean diet is associated with higher cognitive ability and greater brain volume.[44] Panza et al. have suggested that the consumption of Mediterranean diet might act synergistically with other protective factors to prevent and treat cognitive decline.[45] Such diets can be provided as ω- 3 fatty acids, folic acid, carotenoids and vitamin E, which are related to maintaining healthy brain structure and function.[46] A recent double-blind, placebo-controlled, randomized, human intervention study has demonstrated a beneficial effect of flavonoid and polyphenol on cognitive function.[47] Besides, increasing intake of blueberries and strawberries has also been found to slow the rate of cognitive decline through its supplemental intake of anthocyanin and flavonoid.[48]

Furthermore, with the increase of age, tooth loss and chewing inability might also be one of the factors leading to the decline of cognitive ability in the elderly.[49] Chewing might be a protective factor for cognitive decline because it is associated with increased blood flow in specific brain regions.[50] Although the mechanisms involved in the influence of diet on cognitive function are not clear, nutritional status are likely to be involved in the change of neuronal plasticity and

Characteristics	Centenarians (*n* = 412)	Oldest-old adults (*n* = 534)	*P*
Age (year)	102(101,104)	84(82,88)	<0·001
Gender, *n* (%)			<0·001
Males	80(19·4)	214(40·1)	
Females	332(80·6)	320(59·9)	
BMI (kg/m^2)	18(16,20)	20(18,23)	<0·001
BMI <18.5 kg/m^2	222(53·9)	138(25·8)	<0·001
BMI 18.5 kg/m^2 to 24 kg/m^2	167(40·5)	281(52·6)	
BMI ≥24 kg/m^2	23(5·6)	115(21·5)	
Education degree, *n* (%)			<0·001
Illiteracy	374(90·8)	399(74·7)	
Elementary school level	30(7·3)	92(17·2)	
Junior high school level	8(1·9)	43(8·1)	
Living alone, *n* (%)	59(14·3)	101(18·9)	0·062
Mental labour, *n* (%)	5(1·2)	25(4·7)	0·003
Smokers, *n* (%)	36(8·7)	71(13·3)	0·028
Drinkers, *n* (%)	49(11·9)	83(15·5)	0·108
Hypertension, *n* (%)	309(75·0)	374(70·0)	0·091
Diabetes, *n* (%)	38(9·2)	57(10·7)	0·462
CAD, *n* (%)	15(3·6)	41(7·7)	0·009
Anaemia	174(66·4)	88(33·6)	<0·001
White blood cell (109/L)	5·93(5·05,7·14)	6·15(5·10,7·24)	0·321
Neutrophil (109/L)	0·55(0·48,0·63)	0·56(0·49,0·62)	0·614
Lymphocyte (109/L)	0·32(0·25,0·38)	0·31(0·25,0·37)	0·616
Albumin (g/L)	39·2(36·4,41·6)	42·5(40·2,44·2)	<0·001
C-reactive protein (mg/dL)	0·16(0·07,0·39)	0·13(0·06,0·33)	0·057
RDW (%)	14·2(13·4,15·2)	13·9(13·2,14·9)	0·002
MCV	92·5(87·1,96·0)	93·7(88·7,97·2)	0·004
MCHC	313·0(306·0,320·0)	316·0(306·0,323·0)	0·019
Blood glucose (mmol/L)	4·83(4·23,5·64)	4·36(3·82,5·31)	<0·001
ALT	9·55(7·70,12·48)	12·50(10·00,15·90)	<0·001
AST	20·90(18·20,25·10)	22·10(19·20,26·43)	0·001
MMSE	9(5,13)	14(10,20)	<0·001
PNI	39·2(36·4,41·6)	42·5(40·2,44·2)	<0·001
MNA-SF	8(7,9)	10(9,11)	<0·001

***Table 5*: Characteristics of centenarian and oldest-old adults.**
Abbreviations: BMI: body mass index; CAD: cardiovascular diseases; RDW: red blood cell distribution width; MCV: mean corpuscular volume; MCHC: mean corpuscular haemoglobin concentration; ALT: alanine aminotransferase; AST: aspartate aminotransferase; MMSE: mini-mental state examination; PNI: prognostic nutritional index; MNA-SF: mini nutrition assessment-short form.

cognitive function.[51] To achieve a normal cognitive function, it is essential to reduce malnutrition.

Tyas et al. have demonstrated that preventing cognitive decline is critical for the maintenance of healthy ageing.[52] Age and educational level are determinants of cognitive ageing and decline.[53] With males as the reference group, this study found that females were more likely to have cognitive decline than males because females had lower educational levels and performed less mental labour. As recommended by the World Health Organization, the best ways to prevent cognitive decline include participation in mental work and social activities, as well as the consumption of healthy diet to achieve balanced nutrition.[54]

This study had several strengths. First, we focused on specific populations: centenarians and oldest-old adults. Second, we analysed the interesting and valuable relationship between nutritional status and cognitive decline. Third, we presented findings of a large-scale epidemiological study. However, there were several limitations. First, being a survey conducted among specific populations in Hainan Province, China, the findings of this study might not be generalisable to all populations. Second, although surveying the oldest-old adults required huge efforts, the sample size in this study was not enough to make significant inferences among Chinese oldest-old adults. Third, nonresponse rates and self-reporting bias might affect the inferences, as well

as poor transportation and communication. We tried to avoid this by using full census, household survey, and objective data; and by ensuring full communication with local language. Finally, other variables and tools for assessing nutritional status were not included due to the limitation of the variables in this study.

The findings of this study indicated that malnutrition had positive associations with cognitive decline among Chinese centenarians and oldest-old adults. It is therefore important for clinicians and community health workers to pay attention to malnutrition in these populations and provide supplemental nutrients to prevent cognitive decline.

Data sharing statement

Data underlying this study are available within the manuscript.

Contributors

SF, YZ, YY and WY contributed to the study design; SF, YZ and YY conducted the data collection; SF, LF, ZC, XQ and YZ did the statistical analyses; SF and LF wrote the first draft of the report. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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Declaration of interests

The authors declare no conflict of interest.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2022.101336.

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