ASSOCIATION OF ANEMIA WITH ACTIVITIES OF DAILY LIVING IN CHINESE FEMALE CENTENARIANS

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Abstract: *Objectives:* Although anemia and activities of daily living (ADL) disability in female elderly are common conditions and are more likely to occur as people age, little is known about the association of anemia with ADL in female centenarians. The objective of this study was to examine the relationship between anemia and ADL disability in Chinese female centenarians. *Design, setting and participants:* We conducted a population-based cross-sectional study of a sample of 822 Chinese female centenarians from 2014 to 2016. *Measurements:* Blood analysis, home interview, and physical examination were performed following standard procedures. ADL disability was defined as a Barthel Index total score≤60. *Results:* The prevalence of anemia and ADL disability were 66.8% and 29.7% respectively in Chinese female centenarians. Multiple logistic regression analyses revealed that inflammation (OR = 2.280, 95% CI, 1.524-3.410), underweight (OR = 1.653, 95% CI, 1.186-2.303), anemia (OR = 1.775, 95% CI, 1.250-2.521), and living with family (OR = 0.518, 95% CI, 0.302-0.888) were significant factors related to ADL disability. Centenarians with severe anemia had an approximately fourfold greater likelihood of ADL disability than those without anemia (OR =3.747; 95% CI 1.525–9.206). An apparent dose-response relationship was found between anemia and ADL disability. *Conclusion:* These findings may provide some insights into targeted intervention for maintaining ADL independence in female centenarians, especially encouraging the interventions of anemia to improve ADL.

Key words: Anemia, hemoglobin, activities of daily living, Chinese female centenarians.

Introduction

The population aged 80 years or over, including octogenarians and centenarians, has become the fastest-growing age group in the world, especially in China (1). Aging is often associated with a higher risk of physical function limitations (2). Physical function is often measured by activities of daily living (ADL), which can prove the ability to live independently. ADL declines can increase hospitalization and mortality rates, placing a high burden on individuals, family members and care professionals (3-5). Consequently, it is vital to prevent or manage ADL decline to improve quality of life and reduce the mortality rate.

Previous studies have shown that the oldest old are more likely to have ADL disability (6-10). In fact, centenarians are more vulnerable to ADL disability with advanced age. Effective interventions for maintaining ADL independence not only prevent negative outcomes but also reduce individual and social burden (11-13). ADL disability is associated with many nutritional factors among older people (14-16), there is a further study to clarify these factors among centenarians.

As a nutritional risk factor, anemia is a common but never normal concomitant of aging (17). The prevalence of anemia can reach 30.7% in patients older than 80 years, 37% in patients older than 90 years, and more than 50% in centenarians (18-20). Previous studies have investigated the association between ADL and anemia in older adults (21-24). However, studies on the association between ADL and anemia in centenarians are very rare, especially in developing countries, and the sample sizes are minimal. Centenarians, especially female centenarians, have been a rapidly growing segment of the population in China. Female centenarians are more likely to have ADL disability (10, 25). To date, no other studies have focused on the association between ADL and anemia in Chinese female centenarians. Consequently, there is a need for a better understanding of ADL disability and anemia in the oldest old, particularly in female centenarians.

For these reasons, this study aimed to examine the association between ADL disability and anemia based on a relatively large sample of female centenarians from 2014 to 2016.

Methods

Study population

The participants of this study came from 2014 to 2016 population-based, multidisciplinary CHCCS, one of the largest studies of centenarians. The recruitment and sampling procedures of this complete sample study have been previously described (26). Inclusion criteria of this study include the following: (1) women who were 100 years old or older by 1 December 2016; (2) women who volunteered to participate in the study and provided written informed consent; and (3) women who were conscious and were able to complete the home interview, physical examinations, and blood tests. Exclusion criteria of this study include the following: (1)

personal identity information was not complete or the ID card showed an age of <100 years; and (2) refused to comply with the requirements of the study, including the collection of physical information or blood samples. In total, there were 1002 eligible centenarians. 822 female centenarians were included in the final analysis.

This study's protocol was approved by the ethics committee of the Hainan branch of the Chinese People's Liberation Army General Hospital (number 301hn11201601). It complied with the Declaration of Helsinki (seventh revision, 2013) on medical protocols and ethics.

Measurement

Blood analysis, home interview, and physical examination were performed following standard procedures by the interdisciplinary research team. All assays were performed by qualified technicians without knowledge of the clinical data.

Demographic details (age, marital status, education, ethnicity, smoking habits, drinking habits, and living situation) of the participants were collected during home interviews. Body mass index (BMI) was calculated using the standard formula of weight in kilograms divided by height in meters squared. BMI< 18.5kg/m^2 was recognized as underweight. C-reactive protein (CRP) >0.8 mg/dl was defined as inflammation. Chronic conditions (hypertension, diabetes mellitus, heart disease, chronic obstructive pulmonary disease (COPD)/asthma, and stroke), were identified based on self-reports combined with the medical records of the participants. Hypertension was defined as systolic blood pressure (SBP)≥140 mmHg, diastolic blood pressure (DBP) ≥90 mmHg or normal BP with concomitant use of antihypertensive medications (27). Diabetes mellitus was defined as a fasting blood glucose (FBG) level ≥7.0 mmol/L or taking hypoglycemic drugs/insulin (28).

According to the World Health Organization (WHO) criteria, anemia was defined as a hemoglobin concentration less than 120.0 g/L in women, and anemia is classified by severity into mild (110 g/L to normal), moderate (80 g/L to 110 g/L), and severe anemia (less than 80 g/L).

The Barthel index on the Activities of Daily Living Scale [29]was utilized to evaluate ADL, and its validity has been well established in Chinese older people (30). The Barthel index includes ten self-care items including grooming, bathing, feeding, toilet use, dressing, walking, transferring from bed to chair, stair climbing, bowel control, and bladder control. Each item score is given and summed to the Barthel index total score by two trained doctors blinded to the laboratory results. The Barthel index total score classifies the individuals' level of dependence as follows: severe (0-60), moderate (61-90) and slight dependence or independence for ADL (91-100) (31, 32). In this study, we define ADL disability as the Barthel index total score ≤60 (31).

Statistical analyses

The data are presented as means ± standard deviations or medians for continuous variables and as counts (%) for categorical variables. The differences in the continuous variables of the two groups were compared by Student's t-tests and Mann–Whitney U test. The differences in categorical variables were explored using Chi-square tests or Fisher's exact test. Multiple logistic regression models were used for assessing the independent factors associated with ADL disability. All of the analyses were performed with SPSS software (Version 19.0 for windows, serial number: 5087722; IBM Corporation, Armonk, NY, USA). A 2-tailed p <0.05 was considered statistically significant.

Results

Table 1 summarizes the general characteristics of the 822 Chinese female centenarians by categories of anemia. The prevalence of anemia was 66.8%. The prevalence of ADL disability, moderate ADL, and slight dependence or independence for ADL were 29.7%, 43.1%, and 27.2% respectively. Participants with anemia were more likely to have ADL disability (p <0.001). Significant differences were also found between the participants with and without anemia in terms of BMI, CRP.

Table 1
General characteristics of the 822 female centenarians with and without anemia

Characteristic	Without Anemia	With Anemia	p Value
n	273	549	
Age, mean±SD	102.7 ± 2.7	102.9 ± 2.9	0.309
ADL disability,%	58 (21.2%)	186 (33.9%)	<0.001**
Hemoglobin, g/L, mean±SD	128.2 ± 6.9	104.0 ± 12.3	<0.001**
CRP(IQR)	0.2 (0.1-0.4)	0.2 (0.1-0.6)	0.036*
BMI, kg/m², mean±SD	18.4 ± 3.4	17.6 ± 3.1	<0.001*
Widowed, %	242 (88.6%)	473 (86.2%)	0.318
Illiterate, %	266 (97.4%)	528 (96.2%)	0.348
Han ethnicity, %	244 (89.4%)	483 (88.0%)	0.555
Current smoker, %	2 (0.7%)	8 (1.5%)	0.372
Current drinker, %	22 (8.1%)	38 (6.9%)	0.555
Live with Family, %	231 (84.6%)	487 (88.7%)	0.097
Chronic conditions, %			
Hypertension	207 (75.8%)	413 (75.2%)	0.852
Diabetes mellitus	28 (10.3%)	45 (8.2%)	0.328
Heart disease	9 (3.3%)	24 (4.4%)	0.460
COPD/Asthma	16 (5.9%)	20 (3.6%)	0.143
Stroke	7 (2.6%)	12 (2.2%)	0.734

Note: (1) Abbreviations: BMI, body mass index; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease. (2) * p < 0.05; ** p < 0.001.

Multiple logistic regression analyses revealed that inflammation (CRP> 0.8 mg/dl), underweight (BMI<18.5 kg/m2), anemia, and living with family were significant factors related to ADL disability in this population (Table 2). Participants with inflammation (OR = 2.280, 95% CI, 1.524-3.410), underweight (OR = 1.653, 95% CI, 1.186-2.303), and anemia (OR = 1.775, 95% CI, 1.250-2.521) were more likely to have worse ADL status. Participants with living with family (OR = 0.518, 95% CI, 0.302-0.888) were more likely to have better ADL status.

Table 2
Multivariable logistic regression analysis for the association between factors and ADL disability

Variables	OR (95% CI)	p Value
Age		
100-102	1	
103-116	0.933(0.681-1.280)	0.669
CRP		
≤0.8 mg/dl	1	
>0.8 mg/dl	2.280(1.524-3.410)	<0.001**
BMI		
≥18.5 kg/m2	1	
<18.5 kg/m2	1.653(1.186-2.303)	0.003*
Anemia	1.775(1.250-2.521)	0.001**
Widowed	1.340(0.830-2.162)	0.232
Illiterate	0.757(0.331-1.730)	0.509
Han Ethnicity	1.139(0.675-1.923)	0.625
Current smoker	0.744(0.178-3.110)	0.686
Current drinker	0.510(0.244-1.066)	0.073
Live with Family	0.518(0.302-0.888)	0.017*
Hypertension	1.013(0.706-1.453)	0.943
Diabetes mellitus	1.121(0.642-1.956)	0.689
Heart disease	0.527(0.219-1.269)	0.153
COPD/Asthma	1.227(0.575-2.615)	0.597
Stroke	1.975(0.761-5.122)	0.162

Note: (1) Abbreviations: BMI, body mass index; CRP, C-reactive protein; COPD, chronic obstructive pulmonary disease; OR: odds ratio; CI: confidence interval. (2) * p < 0.05; ** p < 0.001.

Table 3 presents the relationship between anemia and ADL disability. The results of multivariable logistic regression analysis indicated that participants with mild, moderate, and severe anemia were more likely to suffer ADL disability. The adjusted odds ratio (OR) of ADL disability when comparing participants with mild and moderate anemia with participants without anemia were 1.659(95% CI, 1.140-2.412) and 1.762(95% CI, 1.095-2.836) respectively. Centenarians with severe anemia had a greater likelihood of ADL disability than those without anemia (OR =3.747; 95% CI 1.525–9.206). An apparent dose-response relationship was found between anemia and ADL disability in all models (p for trend<0.01). In addition, when included as a continuous variable, the hemoglobin levels were also associated with ADL disability (adjusted OR per 1-unit increase in the hemoglobin levels, 0.983; 95% CI, 0.973-0.993).

Discussion

Since centenarians are poorly overall studied, we need more overall knowledge of the oldest old. To the best of our knowledge, this is the first study to report the association between anemia and ADL disability in Chinese female centenarians. The results of this study showed that Chinese female centenarians with inflammation, underweight, and anemia are more likely to have worse ADL status while those with living with family are more likely to have better ADL status. Based on a relatively large sample of 822 female centenarians, this study may add to the evidence of targeted intervention for maintaining ADL independence in female centenarians, especially encouraging the interventions of anemia to improve ADL.

Previous studies have shown that the prevalence of anemia was 47.8% of 185 Georgian female centenarians (20), 29.3% of 89 Polish female centenarians (19), and 36.8% of 337 Chinese women aged 95 and older (23). The findings of this study showed that the highest overall prevalence of anemia was 66.8% in Chinese female centenarians. This result indicates a relatively higher prevalence of anemia in Chinese centenarians compared with previous studies. In this study, the prevalence of ADL disability, moderate ADL, and slight dependence or independence for ADL were 29.7%, 43.1%, and 27.2% respectively. This finding is consistent with that of previous surveys, showing that the prevalence of ADL disability is high and increases rapidly with age in the oldest old (10, 33-35). Considering the high prevalence and clinical relevance of anemia and ADL disability, Effective interventions may be addressed among female centenarians with anemia and ADL disability.

Penninx et al. found that anemia was associated with disability and decreased physical performance in the elderly (36). The current population-based study also found that anemia was significantly associated with ADL disability in Chinese female centenarians. This result was comparable with other studies (37-39). Furthermore, we found an apparent dose-response relationship between anemia and ADL disability. Centenarians with severe anemia had an approximately fourfold

Table 3
The association between anemia and activities of daily living disability in Chinese female centenarians

Variable	Crude Model		Model 1		Model 2	
	OR (95% CI)	p Value	OR (95% CI)	p Value	OR (95% CI)	p Value
Without Anemia	1		1		1	
Mild anemia	1.739(1.212,2.496)	0.003	1.718(1.193,2.474)	0.004	1.659(1.140,2.412)	0.008
Moderate anemia	2.015(1.284,3.160)	0.002	1.951(1.236,3.078)	0.004	1.762(1.095,2.836)	0.020
Severe anemia	4.718(2.034,10.942)	<0.001	4.749(2.030,11.111)	<0.001	3.747(1.525,9.206)	0.004
P for trend	<0.001		<0.001		0.005	

Note: (1) OR: odds ratio; CI: confidence interval. (2) Model 1: Adjusted for age, illiterate, marital status, ethnicity, current smoker, current drinker, and living situation; Model 2: Adjusted for variables in Model 2 plus BMI, CRP and chronic conditions (hypertension, diabetes mellitus, heart disease, stroke, chronic obstructive pulmonary disease/asthma.).

greater likelihood of ADL disability than those without anemia (OR =3.747; 95% CI 1.525–9.206). These findings suggest that higher levels of hemoglobin were associated with less ADL disability. Because there is little literature that explores this association in female centenarians, we can only speculate on underlying mechanisms. First, the impact of anemia on function and strength decline may be related to reduced muscle oxygenation (40). Second, anemia is considered to be a surrogate marker for underlying overt or subclinical diseases such as inflammation or, chronic kidney disease (41). even though these analyses were adjusted for common chronic conditions, the possibility cannot be excluded that underlying disease resulted in less ADL disability (36).

This study confirmed that underweight was associated with ADL disability (42, 43). Lv et al. also found that the underweight group (BMI <18.5 kg/m^2) showed significantly increased risk of disability in ADL (hazard ratio, 1.34; 95% CI, 1.28-1.41) among Chinese adults age 80 years or older (43). Thus, we should pay more attention to underweight for the prevention of disability in ADL. We also found a significant association between inflammation and ADL disability, which may support the findings of Penninx et al. who also found the link between inflammation and subsequent physical decline [36]. Further studies should be focused on joint health effects of inflammation and anemia on ADL, which may have important physiological implications for the targeted intervention of ADL disability.

Several limitations of this study should be considered in future studies. First, as this was a cross-sectional study design, causal inference is limited. Further longitudinal studies are needed to confirm the association between anemia and ADL disability among centenarians. Second, our participants are unlikely to accurately represent the female centenarians of China, so the generalizability of our results is limited, although a relatively large sample of 822 female centenarians was included. Third, some confounding factors, such as

psychological situations and cognitive status in this study, were not included and hence, potential confounders may remain unrecognized. These factors should be considered in further studies.

Conclusion

In this research, Chinese female centenarians with inflammation, underweight, and anemia had worse ADL status while those with living with family had better ADL status. An apparent dose-response relationship was found between anemia and ADL disability. These findings may provide some insights into targeted intervention for maintaining ADL independence in female centenarians. A better understanding of this association could help in encouraging the interventions of anemia to improve ADL because anemia is a potentially modifiable condition. Future studies may focus on clarifying whether ADL of the oldest old will improve after correction of anemia.

Conflicts of Interest: The authors declare no conflict of interest.

Ethical standards: This study's protocol was approved by the ethics committee of the Hainan branch of the Chinese People's Liberation Army General Hospital (number 301hn11201601). It complied with the Declaration of Helsinki (seventh revision, 2013) on medical protocols and ethics.

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