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SERUM HOMOCYSTEINE LEVELS HAD IMPORTANT ASSOCIATIONS WITH ACTIVITY AND QUALITY OF DAILY LIVING IN CHINESE CENTENARIANS

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Abstract: *Background:* Population aging is an important problem worldwide, with activity and quality of daily living commonly reduced in elderly people. leading to increased hospitalization and mortality rates, and substantial individual and social burdens. *Objective:* This study was designed to investigate the associations of serum homocysteine levels with activity and quality of daily living in Chinese centenarians for the first time. *Participants:* The China Hainan Centenarian Cohort Study was performed in 18 cities and counties of Hainan Province. *Main measures:* Home interview, physical examination and blood analysis were performed in 787 centenarians following standard procedures. *Key results:* The median age was 102 years, ranging between 100 and 115 years. There were 634 females (80.6%) and 153 males (19.4%) in all. The median level of serum homocysteine was 23.80 (18.80-29.90) umol/L, whereas median values of Barthel Index and EuroQol 5 Dimensions were 85(60-95) and 0.661(0.558-0.766), respectively. The centenarians with serum homocysteine levels ≥23.8μmol/L were more likely to had lower values of Barthel Index and EuroQol 5 Dimensions than those with serum homocysteine levels <23.8μmol/L (P<0.05 for all). In multivariate linear regression analyses, serum homocysteine levels were significantly associated with Barthel Index and EuroQol 5 Dimensions (P<0.05 for all). *Conclusions:* Serum homocysteine levels had important associations with activity and quality of daily living in Chinese centenarians. Future research should focus on the value of intervening in serum homocysteine levels by supplying folic acid (vitamin B9) and vitamin B12 on improving activity and quality of daily living in elderly people.

Key words: Activity of daily living, Chinese centenarians, homocysteine, quality of daily living.

Introduction

Population aging is a significant problem both in developed and developing countries, with activity and quality of daily living commonly reduced in elderly people, leading to increased hospitalization and mortality rates, and substantial individual and social burdens (1). Plasma homocysteine levels are frequently elevated in elderly people and associated with increased mortality rate (2, 3). Although the associations of serum homocysteine levels with activity and quality of daily living have recently begun to emerge, studies investigating these associations are scarce and show inconsistent results (1, 4, 5). Heterogeneity of study population, such as the differences between elderly people and other adults, may explain these inconsistent results. Indeed, it is still unclear whether these associations exist in elderly people, especially in Chinese centenarians (6-8).

As China becomes an aging society, reduced activity and quality of daily living become severe challenges to be faced by elderly Chinese people. To our knowledge, no study has reported that serum homocysteine levels are associated with activity and quality of daily living in China, let alone in Chinese centenarians. Hainan is a longevity area with the highest population density of centenarians in China. The China Hainan Centenarian Cohort Study (CHCCS) has a considerable sample size and provides a significant population-based sample of Chinese centenarians. The present study was designed to investigate the associations of serum homocysteine levels with activity and quality of daily living in Chinese centenarians for the first time.

Methods

Study population

The CHCCS was a population-based study with 1,002 centenarians. Its cohort profile has been described previously (9). According to the National Civil Registry, all centenarians were identified by the Hainan Civil Affairs Bureau and enrolled in 18 cities and counties of Hainan Province, China, from July 2014 to December 2016. Age was ascertained from national identification cards, and participants were at least 100 years of age. The following inclusion criteria were used to recruit study participants: (1) was 100 years or older; (2) volunteered to participate in the study and provided written informed consent; and (3) was conscious and could cooperate to complete the home interview, physical examination and blood analysis. Exclusion criteria: (1) personal identity information was not complete or identification cards showed an age of less than 100 years; (2) refused to comply with the requirements of the study, including the collection of physical or blood samples. There were 787 centenarians with complete information in the final analysis. No centenarian took any vitamin supplements or

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Table 1
Characteristics of Chinese centenarians with serum homocysteine levels ≥23.8μmol/L or <23.8μmol/L

Characteristics	Total (n=787)	Homocysteine ≥23.8μmol/L (n=394)	Homocysteine <23.8μmol/L (n=393)	P value
Age (year)	102(101-104)	102(101-104)	102(101-104)	0.878
Females (%)	634(80.6)	300(76.1)	334(85.0)	0.002
Barthel Index	85(60-95)	83(60-95)	85(65-95)	0.013
EuroQol 5 Dimensions	0.661(0.558-0.766)	0.661(0.514-0.766)	0.661(0.569-0.840)	0.042
WC (cm)	75(70-80)	76(71-81)	74(68-80)	0.001
SBP (mmHg)	151(136-170)	152(137-173)	149(135-165)	0.028
DBP (mmHg)	76(67-84)	76(68-85)	75(66-83)	0.172
Triglyceride (mmol/L)	1.04(0.80-1.40)	1.07(0.80-1.46)	1.01(0.80-1.34)	0.071
HDL-C (mmol/L)	1.40(1.18-1.67)	1.38(1.16-1.67)	1.42(1.18-1.68)	0.312
LDL-C (mmol/L)	2.72(2.27-3.26)	2.70(2.27-3.30)	2.74(2.28-3.25)	0.644
FBG (mmol/L)	4.85(4.23-5.76)	4.92(4.25-5.78)	4.82(4.22-5.76)	0.653
Homocysteine (μmol/L)	23.80(18.80-29.90)	29.85(26.38-36.60)	18.80(16.05-21.50)	<0.001

Abbreviations: WC: waist circumstance; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; FBG: fasting blood glucose.

other drugs to affect serum homocysteine levels. The present study was launched according to the guidelines laid down in the Declaration of Helsinki and all procedures were reviewed by Ethics Committee of the Hainan Branch of the Chinese People's Liberation Army General Hospital (Sanya, Hainan; Number: 301hn11201601). Written informed consent was given by all centenarians before participation in the present study.

Standard procedures

Home interview, physical examination and blood analysis were performed following standard procedures. The research team included internists, geriatricians, cardiologists, endocrinologists, nephrologists and nurses. Standard evaluation of activity and quality of daily living was administered by trained doctors who were blinded to the laboratory test results. Activity of daily living was scored according to the Barthel Index (BI) with 10 items (grooming, feeding, dressing, bathing, toilet use, transferring, walking, stair climbing, bowel movements and urinary incontinence) (10). Each item of BI was scored with a given number of points assigned to each level of activity, with higher scores representing higher activity of daily living (11). EuroQol 5 Dimensions (EQ-5D) was used to evaluate the quality of daily living. EQ-5D covered five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Standardized index of EQ-5D was calculated based on Chinese data, with higher scores indicating better quality of daily living (12). Both BI and EQ-5D have been widely used and validated in various populations with good reliability (13). Waist circumstance (WC) was measured with a soft tape in the middle point of the lowest rib and iliac crest. After resting in a supine position for five minutes, systolic and diastolic blood pressures (SBP and DBP) were measured twice on the right arm of centenarians with a one-minute interval. The mean of these measurements was used for the final analysis. Venous blood was drawn for determination of serum homocysteine levels and transported in a chilled bio-transport container (4°C) to our Central Laboratory within four hours. Serum concentrations of triglyceride, high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), fasting blood glucose (FBG) and creatinine were tested using enzymatic assays (Roche Products Ltd, Basel, Switzerland) in a fully automatic biochemical autoanalyzer (Cobas c702; Roche Products Ltd, Basel, Switzerland). All assays were performed by qualified technicians without knowledge of clinical data.

Statistical analyses

Along with descriptive statistics (mean and standard deviation for normally distributed continuous variables, median and interquartile range for non-normally distributed continuous variables or number and percentage for categorical variables), all data were compared with Student's t-test (normally distributed continuous variables), Mann–Whitney U test (non-normally distributed continuous variables) or Chi-square test (categorical variables). Linear regression analyses were applied to evaluate the associations of serum homocysteine levels with BI and EQ-5D in the following three models: model 1 with no adjustment; model 2 adjusted for age and gender; and model 3 adjusted for age, gender, WC, SBP, DBP, triglyceride, HDL-C, LDL-C and FBG. Statistical analyses were performed using Statistical Package for Social Science (SPSS) version 17 (SPSS Inc., Chicago, IL, U.S.). Two-tailed tests had significance levels

Table 2
Associations of serum homocysteine levels with activity and quality of daily living in Chinese centenarians

Characteristics	Models	Standardized β	Standard error	t	P value
Barthel Index	1st	-0.091	0.003	-2.567	0.010
	2nd	-0.101	0.003	-2.867	0.004
	3rd	-0.117	0.003	-3.373	0.001
EuroQol 5 Dimensions	1st	-0.094	0.003	-2.632	0.009
	2nd	-0.103	0.003	-2.906	0.004
	3rd	-0.115	0.003	-3.320	0.001

Notes: Linear regression analyses were performed following these models: model 1 with no adjustment; model 2 adjusted for age and gender; and model 3 adjusted for age, sex, waist circumstance, systolic blood pressure, diastolic blood pressure, triglyceride, high-density lipoproteincholesterol, low-density lipoprotein cholesterol and fasting blood glucose.

of P values<0.05.

Results

The median age was 102 years, ranging between 100 and 115 years. There were 634 females (80.6%) and 153 males (19.4%) in all. The median level of serum homocysteine was 23.80 (18.80-29.90) μmol/L, whereas median values of BI and EQ-5D were 85(60-95) and 0.661(0.558-0.766), respectively. As shown in Table 1, the centenarians with serum homocysteine levels ≥23.8μmol/L were more likely to be males, and had higher levels of WC and SBP, and lower values of BI and EQ-5D, than those with serum homocysteine levels <23.8μmol/L (P<0.05 for all). In the first, second and third models of linear regression analyses (Table 2), serum homocysteine levels were significantly associated with BI and EQ-5D values (P<0.05 for all).

Discussion

Population aging is an accelerating and inevitable trend all over the world. Reduced activity and quality of daily living are frequently observed in elderly people and responsible for increased risk of hospitalization and mortality, and aggravated burdens on individuals and society (1). An elevation of serum homocysteine levels is a common phenomenon in elderly people. Some previous studies have found significant associations of serum homocysteine levels with activity and quality of daily living (14, 15). However, there was no such association in other studies (1,16). Thus, previous studies of these associations are still limited and inconsistent, and further studies are needed to investigate these associations. Ethnicity is possible cause for the inconsistent results, and no study has revealed these associations in Chinese people. Moreover, previous studies have rarely paid attention to these associations in elderly people, let alone in Chinese centenarians (17). The present study confirmed for the first time that serum homocysteine levels had significant associations with activity and quality of daily living in Chinese centenarians.

Based on the evidence described above, it is very likely, especially in elderly people, that serum homocysteine levels were significantly associated with activity and quality of daily living, mostly depending on folic acid (vitamin B9) and vitamin B12 (18). Insufficient amounts of folic acid (vitamin B9) and vitamin B12 limit the conversion of homocysteine into methionine (1). Intestinal absorption of food constituents decreases with aging and is probably one of the factors raising serum homocysteine levels, although genetic polymorphisms may also lead to metabolic disturbances (19). Several studies of elderly people have shown the deficiencies in folic acid (vitamin B9) and vitamin B12, and an elevation in serum homocysteine levels (20). Supplying these vitamins appears to decrease serum homocysteine levels in previous study (21). Serum homocysteine levels should be kept within a safe range by continuous supplementation, potentially improving activity and quality of daily living although direct evidence for this is lacking (22, 23). Elderly people may benefit from reduced homocysteine levels by supplying folic acid (vitamin B9) and vitamin B12, and achieve a clear improvement in activity and quality of daily living. It should be emphasized that there is a need for long-term studies to observe the efficiency and safety of intervening in serum homocysteine levels by supplying folic acid (vitamin B9) and vitamin B12, with the aim of improving activity and quality of daily living.

In summary, the present study demonstrated for the first time that serum homocysteine levels had significant associations with activity and quality of daily living in Chinese centenarians. Future research should focus on the value of intervening in serum homocysteine levels by supplying folic acid (vitamin B9) and vitamin B12 on improving activity and quality of daily living in elderly people.

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Consent for publication: Not applicable.

Ethical approval: All the patients were informed about the purposes of the study and consequently have signed their "consent of the patient". All investigations conformed to the principles outlined in the Declaration of Helsinki and were performed with permission by the responsible Ethics Committee of the Hainan Branch of the Chinese People's Liberation Army General Hospital (Sanya, Hainan; Number: 301hn11201601).

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