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Association between early life exposure to the great famine and possible sarcopenia in older Chinese adults: a national cross-sectional study

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ABSTRACT

Objectives We used data from the China Health and Retirement Longitudinal Study (CHARLS) to investigate how an early life famine exposure affected possible sarcopenia (PS) and to explore the extent to which a sex difference exists in the association among older Chinese adults, as well as whether risk factors modify the association.

Design Cross-sectional study.

Setting 28 provinces of China.

Participants Considering that the Great Chinese Famine lasted from the spring of 1959 to the fall of 1961, 3557 participants were selected and categorised into four subgroups based on their date of birth: unexposed group (1 October 1962 to 30 September 1964), fetal exposed group (1 October 1959 to 30 September 1961), infant exposed group (1 January 1958 to 31 December 1958) and preschool exposed group (1 January 1956 to 31 December 1957).

Outcome measure PS was defined as having low muscle strength or low physical performance.

Methods We used multivariable logistic models to analyse the association between early life famine exposure and the risk of PS in elderly life.

Results The prevalences of PS among individuals in the unexposed, fetal, infant and preschool exposed groups were 15.1%, 14.4%, 23.6% and 21.9%, respectively. Compared with the unexposed group, the infant (OR: 1.55; 95% CI 1.17 to 2.05) and preschool exposed (OR: 1.46; 95% CI 1.17 to 1.82) groups exhibited significantly higher risks of PS. In men, the infant (OR: 2.15; 95% CI 1.40 to 3.31) and preschool exposed (OR: 1.78; 95% CI 1.23 to 2.57) groups were more likely to have PS, but no significant increase was seen in women. In both sexes, prevalence of PS was unrelated to early life famine exposure in the urban, underweight and normal weight subgroups.

Conclusions Early life exposure to the Great Chinese Famine was associated with a higher risk of PS in older adults. Keeping normal nutritional status in elderly life might help avoid the risk of PS, whatever the effect of early famine exposure.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This is the first study using data from a large national epidemiological survey to observe that early life famine exposure is associated with a higher possible sarcopenia (PS) risk in older Chinese populations, especially in men.
- ⇒ There is potential misclassification between the famine exposure subgroups.
- ⇒ Differences in age between the famine exposure subgroups might introduce some confounding.
- ⇒ The endpoint of PS used in this study cannot replace clinical diagnosis of sarcopenia, and might reduce the trustworthiness of the study.

INTRODUCTION

Sarcopenia, a progressive and generalised skeletal muscle disorder involving accelerated loss of muscle mass and function,[1] has been defined as 'age-related loss of muscle mass, plus low muscle strength, and/or low physical performance' by the Asian Working Group for Sarcopenia (AWGS).[2] Sarcopenia is associated with increased adverse outcomes including falls, functional decline, frailty and mortality.[3 4] The prevalence of sarcopenia among older adults worldwide is about 10% without any sex difference,[5] while in Chinese older adults it is 14% among men and 15% in women.[6] Considering that the measurement of muscle mass, which is an indispensable procedure in the diagnosis of sarcopenia, is still a challenge in primary care settings, the AWGS 2019 consensus proposed the term 'possible sarcopenia' (PS), defined as the condition of either having low muscle strength or reduced physical performance, in order to promote early identification of people at risk of sarcopenia and raise awareness of sarcopenia prevention in primary care settings.[2] The prevalence of PS ranges from 15.3% to 46.5% globally, and varies from 38.5% to 46.0% among Chinese older adults (≥60 years of age) according to some cross-sectional studies.[7–10]

The environment in early life seems to have an important influence on the risk of sarcopenia in older age, according to evidences from many observational epidemiological studies. Several studies found that a lower birth weight was linked to lower muscle strength[11 12] and less muscle mass[13] in adulthood and older life. However, conflicting findings were reported. A study in Hong Kong investigated the impact of childhood experience of famine on body composition in later life, but did not find significant association between the experience of famine during late childhood (nearly 10 years) and grip strength or walking speed in elderly life.[14] Moreover, the effect of malnutrition exposure during different stages of early life, such as the fetal and infancy periods, on sarcopenia, may vary. A recent study showed that men who were exposed to the Great Chinese Famine during their fetal stage presented considerably decreased physical function in their later life, but the association was not observed in the other exposed groups.[15] However, the indicator in the previous publication was physical function, which although related to the status of muscle and bone, does not allow diagnosis even for PS. Thus, the question of whether malnutrition exposure during stages of early life would lead to the risk of sarcopenia in older age still remains unanswered.

Considering that men are more sensitive to the environment during their childhood,[16] malnutrition experienced during early life might lead to different health outcomes for the two sexes. A study of a British birth cohort reported that a lower birth weight was associated with reduced grip strength over age 50 years, and this relationship was more pronounced in men.[12] Robinson *et al* found that greater exposure to breast milk in infancy was associated with greater grip strength in adult life only in men.[17] However, previous studies only presented sex difference between early malnutrition and later adult performance: none of them further explored the sex difference in the specific age stages of early malnutrition exposure and later occurrence of PS. Moreover, none of them assessed whether factors such as urban-rural region, nutritional status in later life, and lifestyle elements such as smoking and drinking, which were also independently associated with PS,[2] influenced the association between early malnutrition exposure and later occurrence of PS.

Therefore, in this study, we employed data derived from the China Health and Retirement Longitudinal Study (CHARLS) 2015 wave to investigate the relationship between early life exposure to the Great Chinese Famine and the risk of PS at older age. The Great Chinese Famine lasted from the spring of 1959 to the fall of 1961, affected almost all the Chinese living in mainland China, and caused millions of excess deaths.[18] The long duration of this famine provided us a great chance to explore which early age stages of famine exposure worked for sarcopenia. We hypothesised that the earlier was the exposure to the famine, the greater was the risk of PS in old age, that there would be different manifestations between men and women, and that some modifiers existed. We aimed to investigate the relationship between early life exposure to famine at the fetal, infant and preschool stages, and the risk of PS in elderly life. Additionally, we explored sex differences in the long-term impact of early life malnutrition exposure, as well as whether the risk factors mentioned above would modify this association.

METHODS

Study population

All participants were selected from the 2015 wave of CHARLS. CHARLS is a nationally representative longitudinal survey among Chinese adults aged 45 years or older and their spouses, which involved assessments of social, economic and health circumstances of community residents, performed by the National School of Development in Peking University.[19] The detailed protocol of CHARLS has been published elsewhere.[20] Briefly, the baseline survey of CHARLS was conducted in 2011, in which 17 708 participants from 28 provinces were recruited, and then the respondents were followed every 2 years, through a face-to-face computer-assisted personal interview. All the interviewees were required to provide informed consent. A total of 21 095 individuals were interviewed in CHARLS 2015. In the present study, we first selected participants born between 1 January 1956 and 30 September 1964. To minimise misclassification, we then excluded participants born between 1 January 1959 and 30 September 1959, and participants born between 1 October 1961 and 30 September 1962. As a result, 3557 participants with complete PS information were included in the final analysis according to their date of birth and data integrity (figure 1).

Definition of famine exposed groups

Based on the previous study,[21] the participants were divided into four famine-exposed groups according to birth dates: the unexposed group (1 October 1962 to 30 September 1964), the fetal exposed group (1 October 1959 to 30 September 1961), the infant exposed group (1 January 1958 to 31 December 1958) and the preschool exposed group (1 January 1956 to 31 December 1957).

Measurement of muscle strength

Hand grip strength was used to indicate muscle strength as recommended by AWGS 2019. Hand grip strength was measured by the Yuejian WL-1000 dynamometer (Nantong Yuejian Physical Measurement Instrument Co, Nantong, China) in kilograms.[20] Low muscle strength was defined as hand grip strength <28.0 kg for men and <18.0 kg for women. For each participant the measurement was performed twice for both the left and the right hands while they held the dynamometer at a right angle (90°) and squeezed the handle for a few seconds. The maximum readings were recorded and their average was used as the final value. If the participant was unable to perform grip strength measurement in either hand due to health reasons (swelling, inflammation, severe pain or injury), we used the value measured for the other hand.

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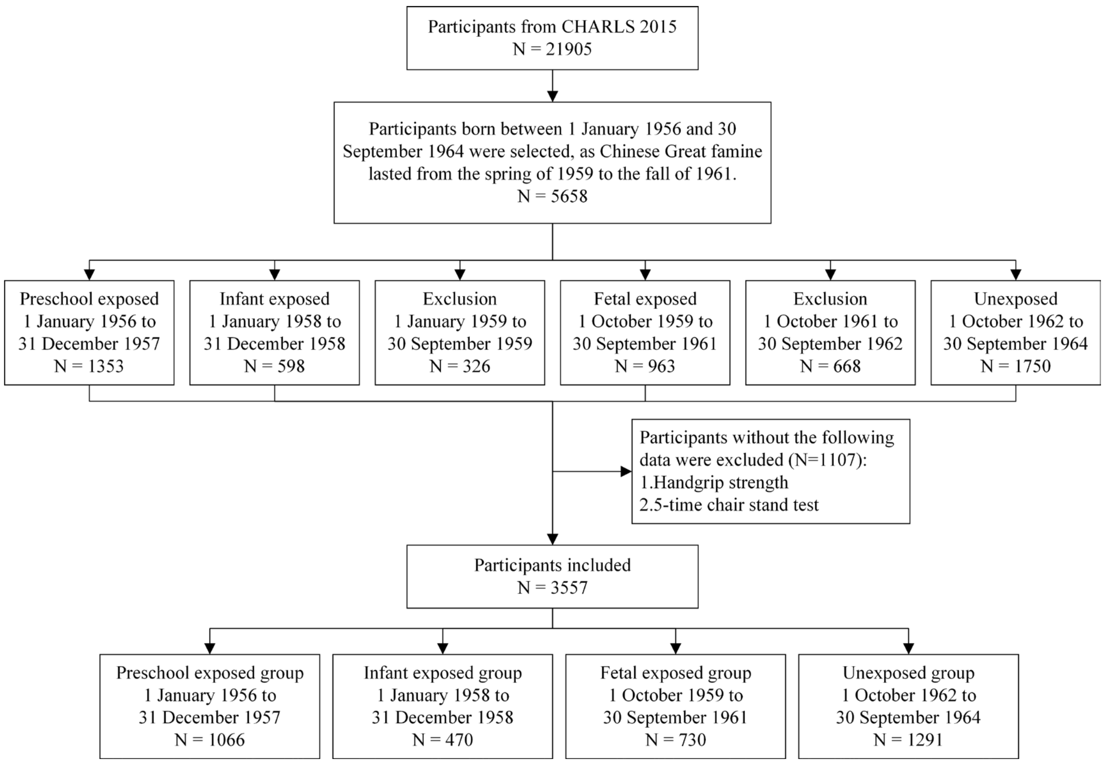

Figure 1 The flow chart of the sample selection of the study. CHARLS, China Health and Retirement Longitudinal Study.

Measurement of physical performance

The 5-time chair stand test was used to assess physical performance, which measures the shortest time needed for the participants to rise continuously five times from the chair without using his or her arms to push off. According to AWGS 2019, low physical performance was defined as 5-time chair stand test ≥12 s.[2]

Assessment of PS

In this study, we adopted the recommended diagnostic algorithm of AWGS 2019.[2] PS was defined as either having low muscle strength or reduced physical performance.

Covariates

As mentioned above, older age, household status, lifestyle, physical inactivity and poor nutritional status are relative factors associated with sarcopenia. Taking that into account, the demographic characteristics in our study included age, sex, region, marital status, education level, economic status, physical activity (PA) level, smoking, drinking, body mass index (BMI) and nutritional status. Region type was classified as urban or rural area according to the residence of participants. Marital status was categorised into married and others (including separated, divorced, widowed, never married and cohabitation). Highest education attainment was categorised into two groups: junior school and below, senior school and above. For economic status, mean family income of the current sample was selected as a threshold to divide all participants into low and high economic status groups.[22] The International Physical Activity Questionnaire - Short Form was used to assess PA level, and PA levels were categorised into low and moderate/high PA level groups, following the recommendation of WHO.[23] Smoking status was categorised into former/current smoker and never smoker (subjects who smoked less than 100 cigarettes in their lifetime). Alcohol use was categorised into former/current drinker, and never drinker. BMI was calculated using weight (kg) divided by height squared (m^2), and the nutritional status of the participants was classified as underweight (BMI<18.5 kg/m^2), normal weight (18.5 kg/m^2≤BMI<24.0 kg/m^2) and overweight (BMI≥24.0 kg/m^2).[24]

Statistical analysis

Continuous variables are reported as means and SD, and categorical variables as counts and percentages. The χ^2 test and analysis of variance were used to compare the differences in categorical variables and continuous variables between the different famine-exposed groups. Logistic regression models were established to analyse the association between famine exposure in early life and PS risk in adulthood. In the complete model, we adjusted for sex, region, marital status, nutritional status, smoking, drinking, education level and economic status. All participants provided complete information on sex, marital status and economic status. Data on region, nutritional status, smoking, drinking and education level were missing in 1.7%, 0.2%, 0.1%, 0.1% and 3.9% participants, respectively. Thus, 3348 subjects were included in the complete model. The missing completely at random (MCAR) test results indicated that there was no difference between the primary sample and the final sample.

Data on PA level were missing in 49.6%, so this variable was not included in the main regression models, but only considered in additional models.

To take account of a multiplicative interaction between the effects of famine exposure and sex on PS risk in elderly life, logistic regression models were also conducted in the sexes separately, adjusting for the confounding variables above. Stratified logistic regression models were also conducted to explore whether urban-rural region, nutritional status, smoking and drinking modified the association.

All statistical analyses were performed using SPSS V.26.0 (IBM Corporation, Armonk, New York, USA). Graphs were drawn using R V.4.0.5 (R Development Core Team, Vienna, Austria). All values of p<0.05 were considered statistically significant.

Sensitivity analysis

In an attempt to reduce age-related bias, we carried out additional logistic regression modelling using data from CHARLS 2011 rather than CHARLS 2015 for the famine-exposed groups (online supplemental table S1).

Patient and public involvement in research

We report no patient or public involvement in the design or implementation of the study.

RESULTS

Characteristics of study participants

A total of 3557 individuals participated in the current study. The prevalences of PS in the unexposed, fetal-exposed, infant-exposed and preschool-exposed groups were 15.1%, 14.4%, 23.6% and 21.9%, respectively. Compared with the unexposed group, the infant exposed and preschool exposed groups had higher prevalence of PS (p<0.001). The distributions of sex, marital status, nutritional status, smoking, education level, economic status and the mean BMI of participants significantly differed between the four groups (p<0.05) (table 1).

Associations between early life famine exposure and the risk of PS

As shown in table 2, the older adults from the infant exposed group (OR: 1.55; 95% CI 1.17 to 2.05) and the preschool exposed group (OR: 1.46; 95% CI 1.17 to 1.82) had significantly higher risks of PS than the unexposed group, even after adjusting for sex, region, marital status, nutritional status, smoking, drinking, education level and economic status. However, no statistically significant difference was found between the fetal exposed and unexposed groups (p=0.493), a conclusion that remained true after additional adjustment for PA, (though based on a smaller sample), where the ORs (95% CIs) were 0.77 (0.51–1.16) for fetal exposure, 1.81 (1.21–2.69) for infant exposure and 1.54 (1.12–2.14) for preschool exposure. In the sensitivity analysis making the average age of the exposed groups closer to that of the unexposed group, all of the famine exposure groups were associated with an increased risk of PS (online supplemental table S1). Additionally, the possibility of a multiplicative interaction between the exposed group and sex was studied. The total interaction test was not significant (p=0.205); however, the interaction between the infant exposed group and sex was significant (p<0.05), which indicated that the famine-sarcopenia association might be sex-specific. In model 4, which adjusts for the interaction of exposed group and sex, the main results of famine exposure accorded with the other models, and the OR of the infant exposed group increased (OR: 3.95; 95% CI 1.55 to 10.03), which indicated that the true effect of famine exposure might be partly masked by the interaction.

Sex difference in the association between famine exposure and the risk of PS

The absolute prevalence of PS in women was higher than it was in men (p<0.001), whereas the difference between sexes in the infant exposed group was not significant (p=0.570). In men, compared with the unexposed group, the fetal exposed group had no significant increased risk (p=0.522), but the infant (OR: 2.15; 95% CI 1.40 to 3.31) and preschool exposed (OR: 1.78; 95% CI 1.23 to 2.57) groups had significantly higher risks of PS in the final adjusted model. However, no statistically significant association was observed between the famine exposure at fetal (p=0.186), infant (p=0.315) or preschool (p=0.054) stages and PS risk among women (table 3).

The associations between famine exposure and PS risk by sex stratified by region, nutritional status, smoking and drinking

As shown in figure 2 and online supplemental table S2, there was no evidence in either sex or overall that fetal exposure was associated with an increased risk of PS. It was also clear that evidence of an association for infant and preschool exposure was stronger in men than in women. Indeed, the only significant increases seen in subgroups in women were for infant exposure in former/current smokers and for preschool exposure in former/current drinkers. While in men many of the associations of infant and preschool exposure with PS were significant, it is notable that no significant associations were seen in those in the urban, underweight and normal weight subgroups.

Additionally, the interactions between the famine exposed groups and region, nutritional status, smoking and drinking were tested respectively, the interaction between famine exposure and nutritional status was significant in men (p<0.05), and the interaction between famine exposure and drinking was significant in both men and women (p<0.05).

DISCUSSION

In this study, we observed a significant association between early life famine exposure and a higher risk of PS in elderly life. Although the absolute prevalence of PS in women was higher compared with that in men, the

Table 1 Basic characteristics of the study population in China according to famine exposure (n=3557)

	Unexposed (n=1291)	Fetal exposed (n=730)	Infant exposed (n=470)	Preschool exposed (n=1066)	*P value*
Birth date	1 October 1962 to 30 September 1964	1 October1959 to 30 September 1961	1 January 1958 to 31 December 1958	1 January 1956 to 12/31/1957	
Female	709 (54.9)	408 (55.9)	227 (48.3)	559 (52.4)	0.040
Rural area	931 (73.6)	556 (77.4)	333 (72.4)	813 (77.1)	0.052
PS	195 (15.1)	105 (14.4)	111 (23.6)	233 (21.9)	<0.001
Marital status					0.003
Married	1240 (96.1)	682 (93.4)	437 (93.0)	989 (92.8)	
Others	51 (3.9)	48 (6.6)	33 (7.0)	77 (7.2)	
PA level					0.178
Low	213 (32.8)	148 (38.9)	165 (68.2)	337 (64.6)	
Moderate/high	436 (67.2)	233 (61.2)	77 (31.8)	185 (35.4)	
Nutritional status					0.001
Underweight	42 (3.3)	24 (3.3)	27 (5.8)	55 (5.2)	
Normal weight	551 (42.8)	328 (45.0)	207 (44.1)	521 (49.0)	
Overweight	695 (54.0)	377 (51.7)	235 (50.1)	488 (45.9)	
Smoking					0.003
Never	786 (61.0)	428 (58.6)	257 (54.7)	574 (53.9)	
Former/current	503 (39.0)	302 (41.4)	213 (45.3)	492 (46.1)	
Drinking					0.362
Never	789 (61.2)	468 (64.2)	289 (61.8)	685 (64.3)	
Current	500 (38.8)	261 (35.8)	179 (38.2)	381 (35.7)	
Education level					<0.001
Junior school and below	1034 (83.5)	530 (75.7)	375 (82.8)	886 (84.2)	
Senior school and above	204 (16.5)	170 (24.3)	78 (17.2)	162 (15.8)	
Economic status					<0.001
Low economic status	890 (68.9)	558 (76,4)	350 (74.5)	848 (79.5)	
High economic status	401 (31.2)	172 (23.6)	120 (25.5)	218 (20.5)	
Age (years)	51.79±0.65	54.80±0.66	57.00±0.00	58.51±0.50	<0.001
BMI (kg/m^2)	24.64±3.82	24.62±4.71	23.97±3.70	23.89±3.51	<0.001

Data are shown as numbers (percentages), or means±SD.
BMI, body mass index; PA, physical activity; PS, possible sarcopenia.

significant association between infancy famine exposure and PS was seen only in men, suggesting that men may be more sensitive than women to the effect of an early life famine exposure on the risk of elderly sarcopenia. In addition, in the normal weight subgroup, any effect of famine exposure seemed to be slight, suggesting that appropriate nutritional status may be important for sarcopenia prevention.

Previous studies showed that lower birth weight or childhood weight were associated with lower muscle strength in adulthood,[11 12] which implied that the early life stages could be critical periods for the mass and quality of skeletal muscle in later life. However, no studies have directly assessed the effects of malnutrition exposure in different early life stages on the risk of sarcopenia at older age. From our knowledge, this study is the first to report that the experience of famine in the infant stage is associated with a higher risk of PS in later life. Indeed, although a few previous studies have investigated the association between famine exposure and objective measures of muscle strength and physical capability, their results were not consistent with ours. A study in Hong Kong did not find any significant association between experience of famine during late childhood and grip strength or walking speed in elderly life.[14] A recent study showed that men exposed to the Great Chinese Famine presented considerably decreased physical function in their later life, but the association was only seen in the fetal exposed group.[15] This discrepancy could be explained by the fact that we used a composite score involving muscle strength and physical performance to assess sarcopenia, whereas the two previous studies used a single indicator. Scores

Table 2 Associations between famine exposure and PS risk

Models	Unexposed (n=1291)	Fetal exposed (n=730)	Infant exposed (n=470)	Preschool exposed (n=1066)
Model 1				
OR (95% CI)	Ref.	0.94 (0.73 to 1.22)	1.74 (1.34 to 2.26)	1.57 (1.27 to 1.94)
P value		0.661	<0.001	<0.001
Model 2				
OR (95% CI)	Ref.	0.94 (0.73 to 1.22)	1.79 (1.38 to 2.33)	1.59 (1.29 to 1.97)
P value		0.639	<0.001	<0.001
Model 3				
OR (95% CI)	Ref.	0.90 (0.69 to 1.19)	1.55 (1.17 to 2.05)	1.46 (1.17 to 1.82)
P value		0.493	0.002	0.001
Model 4				
OR (95% CI)	Ref.	1.72 (0.66 to 4.49)	3.95 (1.55 to 10.03)*	2.36 (1.08 to 5.16)
P value		0.271	0.004	0.031

Model 1, crude model. Model 2, adjusted for sex. Model 3 further adjusted for region, marital status, nutritional status, smoking, drinking, education level and economic status. Model 4 further adjusted for the interaction of exposed group and sex.
*A significant multiplicative interaction was observed between the infant exposed group and sex (p<0.05).
PS, possible sarcopenia; Ref, reference.

derived from a single test are likely to be more unilateral than scores derived from composite tests.

The effect of infancy growth on sarcopenia was probably related to the huge nutritional requirements during infant stage, especially for protein, the substrate for muscle growth.[25] The development of the skeletal muscle can be divided into a series of temporally overlapping phases beginning with the formation of the somites of the early embryo and culminating in the fully differentiated tissue in the adult,[26] and specific cellular events that are affected at each stage differ. The most rapid growth phase occurrs in the infant period, resulting in the expansion of muscle mass from 25% of lean mass at birth to 40%–45% at maturity.[27] Therefore, the infancy stage is a critical window for muscle growth which, if disrupted, results in muscle mass deficits that are unlikely to be entirely recoverable.

After stratifying by sex, we found that the absolute prevalence of PS was higher in women, consistent with previous studies on Chinese older adults.[9] The disparity between the sexes may be due to significant differences in body composition: women have higher body fat, lower muscle mass and greater muscle fat infiltration than men.[28] High body fat has been shown to be associated

Table 3 Associations between famine exposure and possible sarcopenia (PS) risk by sex

	Prevalence N (%)	Model 1		Model 2	
		Or (95% CI)	*P value*	Or (95% CI)	*P value*
Male					
Total	250 (15.1)				
Unexposed	62 (10.7)	Ref.		Ref.	
Fetal exposed	37 (11.5)	1.09 (0.71 to 1.68)	0.699	1.16 (0.74 to 1.83)	0.522
Infant exposed	60 (24.7)	2.75 (1.86 to 4.07)	<0.001	2.15 (1.40 to 3.31)	<0.001
Preschool exposed	91 (17.9)	1.84 (1.30 to 2.60)	0.001	1.78 (1.23 to 2.57)	0.002
Female					
Total	394 (20.7)				
Unexposed	133 (18.8)	Ref.		Ref.	
Fetal exposed	68 (16.7)	0.87 (0.63 to 1.20)	0.381	0.80 (0.57 to 1.12)	0.186
Infant exposed	51 (22.5)	1.26 (0.87 to 1.81)	0.222	1.21 (0.83 to 1.77)	0.315
Preschool exposed	142 (25.4)	1.48 (1.13 to 1.93)	0.004	1.32 (1.00 to 1.74)	0.054

Model 1, crude model. Model 2, adjusted for region, marital status, nutritional status, smoking, drinking, education level and economic status.
Ref, reference.

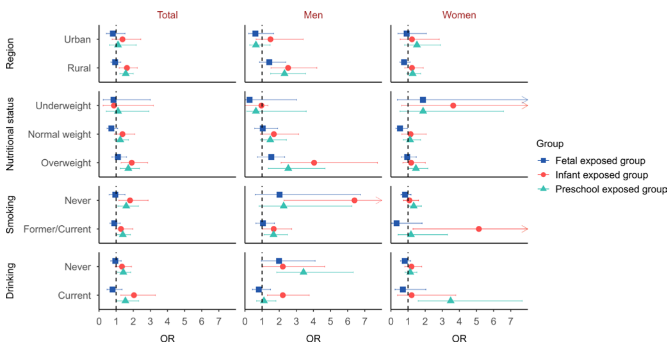

Figure 2 Associations between famine exposure and possible sarcopenia (PS) risk by sex, stratified by region, nutritional status, smoking, drinking. Some OR 95% CIs are too large to show, as indicated by the right arrow.

with poorer physical performance in older adults,[29] and fat accumulation within the skeletal muscle is associated with muscle weakness.[30] However, the association between infant famine exposure and increased risk of PS was only seen in men, which indicates that men are more sensitive to the effect of early life famine exposure on the risk of sarcopenia than women. Although the mechanisms for sex difference existing in the association between famine exposure in early life and the risk of sarcopenia are unclear, several potential mechanisms might contribute to explain the association. First, the sex-specific association might be related to the different influence of sex hormones, such as testosterone, which has anabolic effects on muscle and function.[31 32] It has been reported that birth weight or weight gain in childhood are positively related to testosterone levels in adulthood among men.[33] Another explanation could be the sex differences in skeletal muscle metabolism. Women have higher metabolic flexibility in which substrate oxidation is readily adapted by nutrient availability.[34]

Additionally, we also found that for both sexes, the three exposed groups showed no increased risk of PS compared with the unexposed group in the urban, underweight and normal weight subgroups. The reason why results differed in urban and rural areas might be that food supply and livelihood security in urban areas is better than in rural areas even during the famine period. As for the underweight subgroup, underweight itself is an important risk factor of sarcopenia,[35] so it is possible that underweight people are at a high risk of developing sarcopenia regardless of whether they have experienced famine or not. In the normal weight subgroup the three exposed groups showed no increased risk of PS compared with the unexposed group, which might suggest that keeping proper weight in elderly life might help avoid the risk of sarcopenia regardless of the early famine exposure, especially for men. Strong evidence has shown that appropriate nutritional status is an important factor affecting the risk of sarcopenia for older adults, and it is also the focus of preventive strategies to date.[36] Sarcopenia, as is well known, is an age-related skeletal muscle disorder. Nowadays, the ageing degree of China's society is deepening apace. By the end of 2021, there were 200.56 million people aged 65 years and over in China, accounting for 14.2% of the national population.[37] According to the internationally accepted classification standard, China has entered a deeply ageing society. About 28.08 million Chinese people might suffer from sarcopenia and its subsequent converse outcomes including falls, functional decline, frailty and mortality,[3 4] and such a situation would worsen considering the accelerating ageing society of China. Therefore, implementing appropriate interventions to prevent sarcopenia is of great importance for improving health status and reducing the burden of healthcare among Chinese people. Furthermore, appropriate interventions targeted towards maintaining normal weight should be recommended for the entire older adult population who have experienced childhood famine or similar food insecurity, especially for men, for compensating their earlier adversity and improving future life quality. Today, people's living standard has been greatly improved, the probability of large-scale famine is low, but food insecurity was still widespread all over the world, especially in low-income countries.[38] Although the damage caused by early life malnutrition is unlikely to be entirely recoverable, interventions in adulthood and older age could play an important role in sarcopenia prevention.[39] Besides, providing opportunity for intervention at a younger age might be beneficial, when lifestyle changes such as regular PA and optimal diet might be easier to implement.[40] Therefore, the optimal nutritional status in both early life and adulthood are crucial for the quantity and quality of skeletal muscle in older age, and linking a life course approach might have the potential to be an effective way to develop targeted treatments and preventive strategies.

To the best of our knowledge, this is the first study using large national epidemiological survey data that observed that infancy famine exposure is associated with a higher PS risk in Chinese older men, and that the effect of famine exposure seems to be slight in those participants with appropriate nutritional status. Our result reinforces the importance of considering the health implications of early malnutrition and the necessity to develop both prevention programmes aimed at reducing them and prevention interventions to mitigate their negative impact over the life course. However, several limitations of our work should be mentioned. First, there is potential misclassification between the famine exposure subgroups. Like previous studies on the Chinese famine,[21] we used participants' date of birth to distinguish famine exposure. But the timing and severity of the Great Chinese Famine varied, and individual famine exposure records were absent. To minimise potential misclassification, we excluded those participants born in the junction of the famine exposure subgroups. Second, 1107 participants without outcome information were excluded, but the MCAR test results of the sample indicated that missing outcome information was more likely in urban and male participants, which might introduce some bias in the results of our analysis. Third, an effect of age differences between famine exposure subgroups exists, which might inevitably cause some confounding of our results. Fourth, the total interaction between the famine exposed group and sex was significant in the univariate logistic regression model, but due to sample size limitations, the interaction is not significant when other variables were adjusted, so our clues need to be confirmed by larger sample studies. Fifth, our use of PS in this study rather than clinical diagnosis might have reduced its trustworthiness.

CONCLUSION

In conclusion, we find that early life exposure to the Great Chinese Famine is associated with a higher risk of PS in elderly life. The effect of exposure to famine in early life on sarcopenia might differ by sex and by nutritional status. Keeping normal nutritional status in elderly life might help avoid the risk of sarcopenia whatever the effect of early famine exposure, and thus appropriate interventions targeted towards maintaining normal weight should be recommended for the entire older adult population that experienced childhood famine or similar food insecurity. However, as this was the first study to assess the association between early life famine exposure and PS in older age, and the sample size of our study was limited, larger sample research is needed to confirm our findings.

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