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Associations of early-life exposure to famine with abdominal fat accumulation are independent of family history of diabetes and physical activity

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Abstract

The present study aimed to investigate the association of early-life exposure to famine with abdominal fat accumulation and function and further evaluate the influence of first-degree family history of diabetes and physical activity on this association. The present work analysed parts of the REACTION study. A total of 3033 women were enrolled. Central obesity was defined as waist circumferences (W) ≥ 85 cm. Chinese visceral adiposity index (CVAI) was used to evaluate visceral adipose distribution and function. Partial correlation analysis showed BMI, W, glycated Hb and CVAI were associated with early-life exposure to famine (both $P < 0{\cdot}05$). Logistic regression showed that the risks of overall overweight/obesity and central obesity in fetal, early-childhood, mid-childhood and late-childhood exposed subgroups were increased significantly (all $P < 0{\cdot}05$). Compared with the non-exposed group, the BMI, W and CVAI of fetal, early- to late-childhood exposed subgroups were significantly increased both in those with or without first-degree family history of diabetes and in those classified as physically active or inactive, respectively (all $P < 0{\cdot}05$). The associations of BMI, W and CVAI with early-life exposure to famine were independent of their associations with first-degree family history of diabetes (all $P < 0{\cdot}01$) or physical activity status (all $P < 0{\cdot}001$). Early-life exposure to famine contributed to abdominal fat accumulation and dysfunction, which was independent of the influence of genetic background and exercise habits. Physical activity could serve as a supplementary intervention for women with high risk of central obesity.

Key words: **Early-life exposure to famine: Abdominal fat: Family history of diabetes: Physical activity: Chinese visceral adiposity index**

Famines, like the Dutch famine which occurred at the end of the Second World War and which has been fully studied, provide researchers with a quasi-experimental setting to investigate the long-term impact of nutritional deprivation during gestation and childhood on adult health outcomes[1]. With a duration of about 3 years, the Chinese famine of 1959–1961 was longer and larger than any other historical famine in recorded human history, leading to approximately 30 000 000 excess deaths[1,2]. Grain production yielded a sudden and drastic decline in 1959–1961, which was an immediate cause of the famine. A series of natural and social factors such as drought, delayed response to the food shortage and resource diversion due to massive industrialisation compounded the food shortage and exacerbated the famine[1].

This famine exerted profound influence on the health of the Chinese population. Nutrition in early life, to a great extent, determines adult health[2]. The developmental origins of health and disease theory proposed that the physical and structural changes in response to malnutrition, which are involved in survival during early life, might predispose individuals to metabolic diseases and CVD in later life[3]. A great numbers of studies have provided evidence that compared with those born after the famine, the population with early exposure to famine in their fetal and childhood periods were more likely to develop metabolic diseases and CVD such as overweight/obesity, type 2 diabetes mellitus, hyperglycaemia, hypertension, dyslipidaemia and fatty liver disease[4–6].

Central obesity is recognised as not only a fundamental pathology for the metabolic syndrome but also an important factor associated with the onset and progression of the important chronic non-communicable diseases, such as CVD[7]. Clinical studies revealed that early-life exposure to famine increased the risk of central obesity, which in turn intensified and

Abbreviations: CVAI, Chinese visceral adiposity index; FDR, first-degree relative; W, waist circumference.

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aggravated the risks of metabolic abnormality like diabetes caused by this exposure[6,8]. Our previous studies revealed that first-degree relatives (FDR) of diabetes were more likely to develop metabolic disorders, especially abdominal fat accumulation[9]. Regular exercise and leisure-time exercise with moderate or vigorous intensity were effective for the reduction of intra-abdominal adipose tissue and improvement of glucose metabolism, as well as enhancement of cardiorespiratory fitness[10]. Prevention of central obesity could alleviate the adverse effects of early-life exposure to famine[2]. Up till now, however, there has been no study exploring whether the genetic background (family history of diabetes) and lifestyle intervention (physical activity) would aggravate or ameliorate the adverse physical changes and metabolic consequences of famine exposure, especially central obesity.

When compared with men, women may be more adaptable and more likely to survive famine. The relationship between famine exposure and a lower men:women ratio has been demonstrated[11]. Correspondingly, these surviving women suffered higher risks of metabolic diseases in their later years[3,12]. Several studies uncovered the association between early-life exposure to famine and obesity in adult women rather than men[2,6,12]. Additionally, the unhealthy effects of obesity were more pronounced in women[8]. Therefore, enrolling women as the study population, the present study aimed to investigate the association of early-life exposure to famine with abdominal fat accumulation and function and further evaluate the influence of first-degree family history of diabetes and physical activity on this association.

Subjects and methods

Study population

The present work analysed a portion of the baseline data (Wenzhou and Ningde, located in the south-east of China) of the Risk Evaluation of cAncers in Chinese diabeTic Individuals: a lONgitudinal (REACTION) study. The REACTION study was conducted between 2011 and 2012 among 259 657 adults, who were over 40 years of age in twenty-five communities across mainland China, to investigate the relationship of diabetes and cancer[13]. Women who were born from 1 October 1952 to 30 September 1964 were recruited. In consideration of the unclear date of the start and end of the famine, women who were born between 1 October 1958 and 30 September 1959 or between 1 October 1961 and 30 September 1962 were excluded to minimise the misclassification of the famine exposure. Subjects with the following conditions were excluded: established cardiovascular and cerebrovascular diseases, severe liver or renal dysfunction, acute infection, tumours and psychiatric disease. After exclusion, the final sample size was 3033 for the current analysis.

The present study was conducted in accordance with the Declaration of Helsinki and approved by the Ruijin Hospital Ethics Committee, Shanghai JiaoTong University School of Medicine. All of the participants provided with written informed consents before participation.

Questionnaire interview

The clinical information including demographic characteristics, family history of diabetes and lifestyle indicators such as physical activity, total sitting time per week, smoking and drinking status was self-reported with a standardised questionnaire.

According to the years of famine and self-reported date of birth (which was verified by the information on national identification card)[2], the present study population was divided into a non-exposed cohort (1 October 1962–30 September 1964) and an exposed cohort (1 October 1952–30 September 1961), of which, the latter one were further divided into a fetal exposed cohort (1 October 1959–30 September 1961), early-childhood exposed (1 October 1956–30 September 1958), mid-childhood exposed (1 October 1954–30 September 1956) and late-childhood exposed (1 October 1952–30 September 1954).

Physical activity status was evaluated according to the International Physical Activity Questionnaire[14]. 'Physically active' was defined as undertaking moderate-to-vigorous-intensity physical activity ≥30 min per week, and 'physically inactive' was defined as undertaking moderate-to-vigorous-intensity physical activity <30 min per week[15].

The first-degree family history of diabetes was defined as having at least one FDR (parent, sibling or child) with diabetes[16].

Menopause was defined as ≥12 consecutive months of amenorrhoea without other medical causes[17].

Physical examination

Physical examinations of anthropometric indexes (body height, weight and waist circumference (W)) and blood pressure were performed comprehensively in every participant with standard protocols by trained physicians as previously described[18]. BMI was calculated as weight (kg)/height^2 (m^2). Blood pressure was measured three times at 5-min intervals after participants had been comfortably seated for more than 10 min. The average value of systolic blood pressure and diastolic blood pressure was calculated for the analysis.

Central obesity was defined as W ≥ 85 cm[7].

Laboratory tests

After a fasting at least 8 h, the fasting blood samples were collected to assess fasting plasma glucose, glycated Hb, total cholesterol, TAG, high HDL-cholesterol and low LDL-cholesterol on the auto analyser. Participants without diagnosed diabetes had taken 75 g glucose orally and those with diabetes underwent a 100 g carbohydrate test. A blood sample was collected again after 2 h to detect the 2-h plasma glucose. These methods have been described previously[18].

Chinese visceral adiposity index (CVAI) was used to evaluate visceral adipose distribution and function in the Chinese population, calculated as follows: $\text{CVAI} = -187{\cdot}32 + 1{\cdot}71 \times \text{age} + 4{\cdot}23 \times \text{BMI} + 1{\cdot}12 \times \text{W} + 39{\cdot}76 \times \log_{10}\text{TAG} - 11{\cdot}66 \times \text{HDL-cholesterol}$[19].

Statistical analysis

Statistical analyses were performed with SPSS version 16.0 (SPSS Inc.). For continuous variables, data were presented as mean

values and standard deviations or medians with interquartile ranges, and for categorical variables, data were presented as numbers and percentages. Comparisons between the two groups were carried out by an unpaired Student's t test, Mann–Whitney U test and χ^2 test for continuous and categorical variables, respectively. Logistic regression analysis was performed to evaluate the independent factors associated with exposure to famine, and the relationship between exposures to famine in different periods with central obesity. ANOVA were applied to exploring the interaction on W and CVAI between exposures to famine in different periods and first-degree family history of diabetes or physical activity. All reported P values were two-tailed, and $P < 0{\cdot}05$ was considered statistically significant.

Results

Clinical characteristics of study participants

A total of 3033 women with an average age of 53·42 (SD 3·63) years (age range 46·71–59·22 years) were enrolled in the present study. There are 731 participants without exposure to famine and 2302 participants with early-life exposure to famine, including 423 fetal exposed women, 677 early-childhood exposed women, 647 mid-childhood exposed women and 555 late-childhood exposed women. Compared with non-exposed participants, early-life exposed participants were older and exhibited higher levels of BMI, W, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, 2-h plasma glucose, glycated Hb, total cholesterol, TAG, LDL-cholesterol and CVAI (all $P < 0{\cdot}01$, Table 1). Among different early-life exposed subgroups, age, systolic blood pressure, diastolic blood pressure, W, 2-h plasma glucose, glycated Hb, total cholesterol, TAG, LDL-cholesterol and CVAI differed (all $P < 0{\cdot}05$).

Metabolic factors associated with early-life exposure to famine

In terms of metabolic factors, Spearman correlation analyses were conducted and found that BMI, W, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, 2-h plasma glucose, glycated Hb, total cholesterol, TAG, LDL-cholesterol and CVAI were associated with early-life exposure of famine (all $P < 0{\cdot}001$). However, after adjusted for age and menopause status, only the associations of BMI ($P = 0{\cdot}002$), W ($P = 0{\cdot}009$), glycated Hb ($P = 0{\cdot}016$) and CVAI ($P = 0{\cdot}013$) with early-life exposure of famine remained significant in partial correlation analysis (Table 2).

Associations between obesity and different periods of exposure to famine

Defining the present of overall overweight/obesity as a dependent variable and the non-exposed group as reference, logistic regression showed that the risks of overall overweight/obesity in fetal exposed, early-childhood exposed, mid-childhood exposed and late-childhood exposed subgroups were increased by 36·4, 40·8, 47·7 and 97·1 %, respectively (all $P < 0{\cdot}05$). For central obesity, the risks in fetal-exposed, early-childhood exposed, mid-childhood exposed and late-childhood exposed subgroups were increased by 48·6, 78·3, 120·3 and 171·8 % compared with the non-exposed group, respectively (all $P < 0{\cdot}01$, Fig. 1). After adjustment for physical activity status and first-degree family history of diabetes, the (OR remained increased in fetal exposed, and early- to late-childhood exposed subgroups for overall overweight/obesity (OR 1·361, 1·422, 1·484 and 2·018, respectively, all $P < 0{\cdot}05$) and central obesity (OR 1·470, 1·786, 2·206 and 2·757, respectively, all $P < 0{\cdot}01$).

Impact of first-degree family history of diabetes on the association between indexes of obesity and early-life exposure to famine

W and CVAI (both $P = 0{\cdot}001$) were significantly increased in FDR of diabetes independent of periods of exposure to famine. Compared with the non-exposed group, the BMI of fetal exposed, early-childhood exposed, mid-childhood exposed and late-childhood exposed subgroups was significantly increased by 0·91, 0·54, 0·62 and 1·00 kg/m^2 (all $P < 0{\cdot}05$), the W of these subgroups was increased by 2·51, 3·33, 3·54 and 4·75 cm (all $P < 0{\cdot}001$, Fig. 2(a)) and the CVAI of these subgroups was increased by 12·00, 16·16, 20·60 and 28·79 (all $P < 0{\cdot}001$, Fig. 2(b)) with the impact of first-degree family history of diabetes. The associations of indexes of obesity (BMI, W and CVAI) with early-life exposure to famine were independent of their associations with first-degree family history of diabetes ($P = 0{\cdot}001$ for BMI and <0·001 for W and CVAI, Fig. 2).

Impact of physical activity status on the association between indexes of obesity and early-life exposure to famine

ANOVA revealed that BMI ($P = 0{\cdot}001$), W ($P = 0{\cdot}035$) and CVAI ($P < 0{\cdot}001$) were much lower in women categorised as physically active, compared with those categorised as physically inactive, regardless of the periods of exposure to famine. With the impact of physical activity status, the BMI of fetal exposed, early-childhood exposed, mid-childhood exposed and late-childhood exposed subgroups was significantly increased by 0·98, 0·55, 0·65 and 0·93 kg/m^2 when compared with the non-exposed group (all $P < 0{\cdot}05$). Additionally, the W of fetal and early- to late-childhood exposed subgroups were increased by 2·72, 3·13, 3·90 and 4·65 cm, respectively (all $P < 0{\cdot}001$, Fig. 3(a)), and the CVAI of these subgroups was increased by 14·41, 17·74, 23·14 and 29·67, respectively (all $P < 0{\cdot}001$, Fig. 3(b)) when compared with the non-exposed group. The associations of indexes of obesity with early-life exposure to famine were independent of their associations with physical activity status (all $P < 0{\cdot}001$, Fig. 3).

Discussion

The present study revealed that early-life exposure to famine was associated with obesity, especially central obesity in women. With exposure to famine, during fetal or childhood periods, women's risk of obesity and central adiposity in their fifties would be increased. The association of obesity with first-degree family history of diabetes and its association with early-life exposure to famine were independent significantly of each other.

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Table 1. Characteristics of the study participants
(Medians and interquartile ranges (IQR); mean values and standard deviations)

Metabolic factors	Non-exposed (*n* 731)		Early-life exposure to famine									
			Total (*n* 2302)		Fetal exposed (*n* 423)		Early-childhood exposed (*n* 677)		Mid-childhood exposed (*n* 647)		Late-childhood exposed (*n* 555)	
	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR	Median	IQR
Age (years)	48·22	47·74–48·68	55·24*	53·60–57·04	51·39	50·84–51·78	54·10	53·65–54·51	56·05	55·59–56·64	58·05	57·55–58·57
BMI (kg/m^2)	23·20	21·52–25·05	23·92*	22·03–26·03	23·84	22·37–25·95	23·75	21·85–25·81	23·86	21·99–25·81	24·17	22·02–26·47
W (cm)	78·00	73·00–83·00	81·00*	76·00–87·00	80·00	75·00–85·00	80·00	76·00–86·00	81·00	76·00–87·00	83·00	77·00–88·50
SBP (mmHg)	123·33	114·33–136·33	130·00*	118·33–143·00	127·33	117·00–140·00	128·00	117·00–141·00	130·33	117·33–143·00	135·00	121·33–147·00
DBP (mmHg)	75·67	69·00–83·33	77·67*	70·67–84·33	77·00	71·00–83·00	77·33	70·33–83·33	77·00	70·33–84·33	79·33	72·33–85·33
FPG (mmol/l)	5·30	4·92–5·67	5·38*	5·00–5·84	5·37	5·00–5·78	5·32	4·98–5·82	5·36	4·99–5·83	5·45	5·03–5·92
2hPG (mmol/l)	6·60	5·55–7·70	6·92*	5·82–8·44	6·81	5·74–7·89	6·70	5·69–8·12	6·90	5·84–8·50	7·30	6·09–9·11
HbA1c (%)	5·60	5·30–5·80	5·80*	5·50–6·10	5·70	5·50–6·00	5·80	5·50–6·00	5·80	5·50–6·10	5·80	5·60–6·20
TC (mmol/l)												
Mean	5·04		5·42*		5·30		5·34		5·48		5·54	
SD	1·04		1·08		1·01		1·06		1·09		1·12	
TAG (mmol/l)	1·16	0·86–1·61	1·33*	0·96–1·90	1·30	0·95–1·79	1·25	0·91–1·89	1·36	0·96–1·89	1·40	1·01–2·03
LDL-cholesterol (mmol/l)												
Mean	2·90		3·20*		3·15		3·12		3·24		3·28	
SD	0·80		0·85		0·81		0·84		0·81		0·93	
HDL-cholesterol (mmol/l)	1·42	1·21–1·65	1·41	1·20–1·62	1·43	1·23–1·63	1·41	1·21–1·62	1·41	1·20–1·61	1·40	1·18–1·63
CVAI												
Mean	68·23		89·65*		81·83		86·01		91·15		98·34	
SD	23·61		25·78		23·53		25·27		25·34		25·86	

W, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2hPG, 2-h plasma glucose; HbA1c, glycated Hb; TC, total cholesterol; CVAI, Chinese visceral adiposity index.
* $P < 0{\cdot}01$ *v.* individuals without exposure.

Table 2. Associations between the present of early-life exposure to famine and metabolic factors

	Model 1*		Model 2†	
Metabolic factors	*r*	*P*	*r*	*P*
BMI	0·102	0·001	0·055	0·002
W	0·192	<0·001	0·048	0·009
SBP	0·130	<0·001	−0·007	0·680
DBP	0·065	<0·001	0·004	0·827
FPG	0·073	<0·001	−0·003	0·888
2hPG	0·104	<0·001	−0·004	0·844
HbA1c	0·230	<0·001	0·044	0·016
TC	0·158	<0·001	0·002	0·902
TAG	0·101	<0·001	−0·021	0·258
LDL-cholesterol	0·154	<0·001	0·023	0·214
HDL-cholesterol	−0·017	0·346	−0·021	0·259
CVAI	0·335	<0·001	0·045	0·013

W, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; FPG, fasting plasma glucose; 2hPG, 2-h plasma glucose; HbA1c, glycated Hb; TC, total cholesterol; CVAI, Chinese visceral adiposity index.
* Unadjusted.
† Adjusted for age and menopause status.

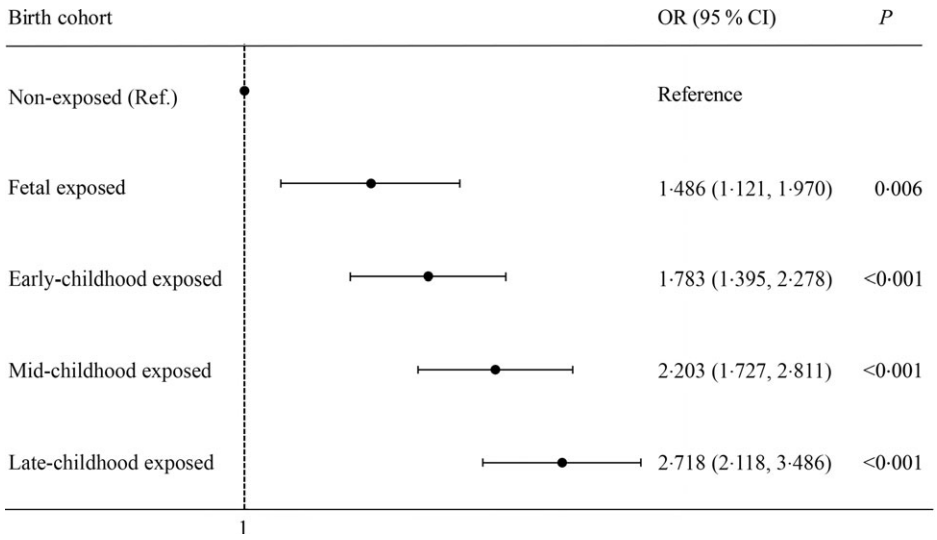

Fig. 1. Associations between central obesity and different periods of exposure to famine. Ref., reference.

Similarly, the association of obesity with physical activity status and its association with early-life exposure to famine were independent significantly of each other.

A study conducted in 35 025 Chinese women reported that the individuals born in 1957 gained 0·92 kg/m^2 in BMI because of famine exposure in their early-childhood compared with those born in the reference non-famine year of 1963. However, the direction of the correlation between BMI and famine exposure was reversed for those born in 1960 and 1961. These findings reflected the different impacts of exposure to famine on obesity in different periods (pregnancy, infancy or childhood)[1]. The China Health and Nutrition Survey compared the data between the cohorts born during and after the famine and found that the prevalence of overweight was higher in the former cohort[20]. Another study based on China Health and Nutrition Survey also demonstrated that compared with those without exposure to famine, individuals born in 1959, 1960 and 1961 had significant increase in BMI and the prevalence of overweight[21]. Chen *et al.* uncovered that in women, individuals with fetal and childhood exposure to famine showed higher BMI, W and visceral adiposity index than those without exposure to famine. After adjustment for potential confounders, the CVAI of fetal and childhood exposed cohorts increased by 15 and 9 %, respectively, when compared with that of the non-exposed cohort[19]. A prospective study lasting 7·3 years found that overall obesity was associated with diabetes among the non-exposed, fetal-exposed and childhood-exposed individuals, and the association between abdominal obesity and famine was pronounced in fetal-exposed individuals[8]. In line with the previous findings, the present study suggested that exposure to famine in fetal development and early childhood increases the risk of abdominal obesity and exacerbates dysfunction of visceral adipose tissue. Given the previous and present findings, the early-life exposure to famine was associated with abdominal obesity and its related metabolic abnormalities in women.

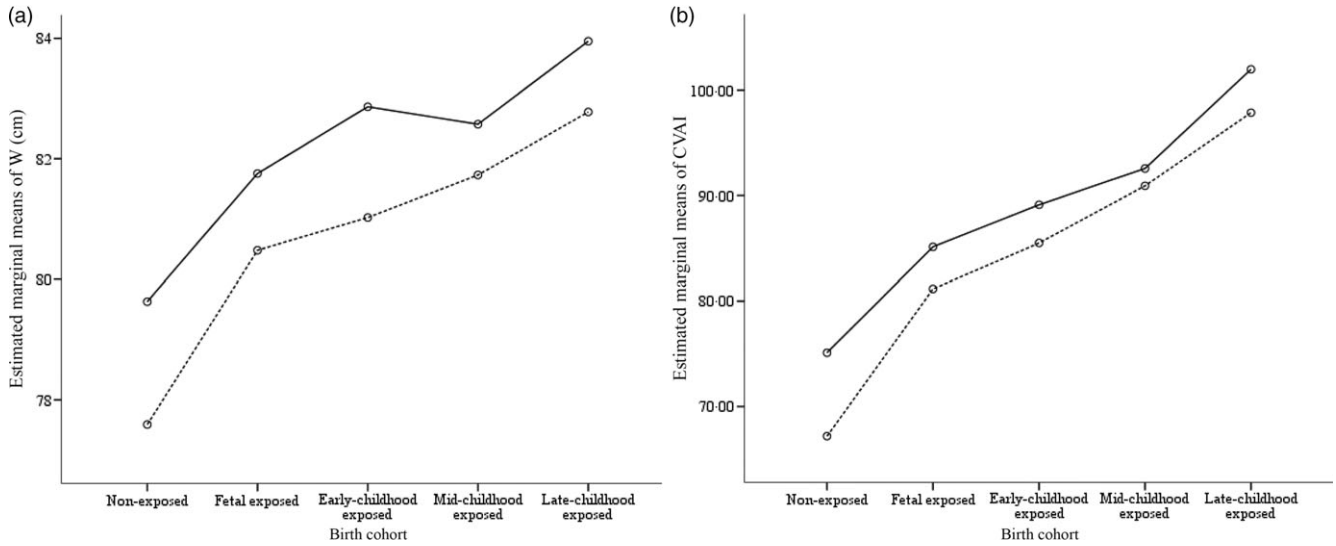

Fig. 2. Impact of family history of diabetes on the association of waist circumference (W) (a) and Chinese visceral adiposity index (CVAI) (b) with early-life exposure to famine. ——, First-degree relatives (FDR); -----, non-FDR.

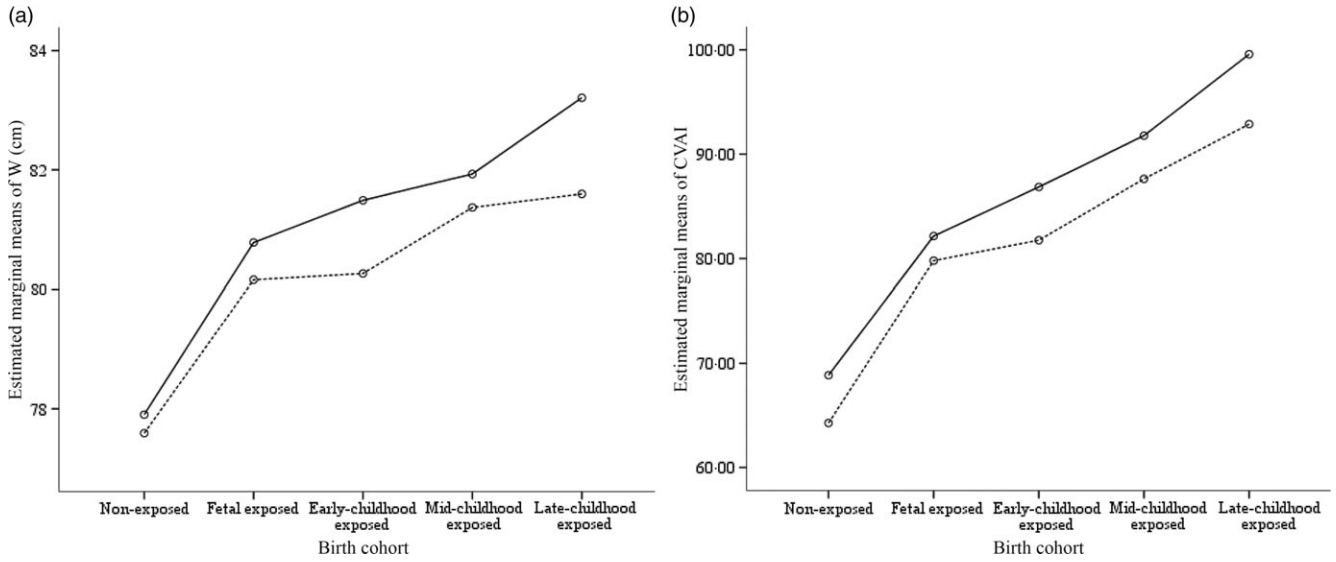

Fig. 3. Impact of physical activity on the association of waist circumference (W) (a) and Chinese visceral adiposity index (CVAI) (b) with early-life exposure to famine. ——, Physically inactive; -----, physically active.

FDR of diabetes exhibit early signs of metabolic abnormalities[22]. American researchers found in those without diabetes, several indexes of obesity, including BMI, total fat mass, percentage body fat, lower body fat mass, visceral and abdominal subcutaneous fat areas, as well as abdominal and femoral adipocyte sizes, were greater in FDR of diabetes than non-FDR of diabetes. Especially for women, the positive first-degree family history of diabetes is an independent predictor of abdominal adipocyte size[23]. Our previous study showed that after adjustment for sex and age, W was significantly increased by 0·86 cm in FDR of diabetes[9]. Consistently, the present study found that FDR of diabetes exhibited higher extent of abdominal fat accumulation and dysfunction, which were further aggravated in those with early-life exposure to famine. Both familial factors and early nutritional factors could exert influence of abdominal fat distribution and function, which were independent of each other and therefore could intensify each other.

Blond *et al.* carried out a 6-month study in individuals with overweight and class 1 obesity and discovered that leisure-time exercise of moderate or vigorous intensity could reduce the W, fat mass and intra-abdominal adipose tissue mass[10]. A study from the Netherlands revealed that for postmenopausal overweight women, subcutaneous and visceral fat was reduced by 12·5 and 12·0 %, respectively, with diet. When combined exercise with diet, the intervention exerted larger impacts on subcutaneous and visceral fat, which was reduced by 16·0 and 14·6 %, respectively. The reduction in subcutaneous fat instead of the visceral fat was statistically and significantly larger in the group

that combined exercise with diet than the diet-only group[24]. The present study also suggested that for those with early-life exposure to famine, being physically active (moderate-to-vigorous-intensity physical activity ≥30 min per week), even with the time of physical activity less than the time (≥150 min/week during 3–5 daily sessions per week) for patients with obesity recommended by the American Association of Clinical Endocrinologists and American College of Endocrinology[25], could contribute to the reduction in the W and improvement of function of intra-abdominal adipose tissue. However, for those with moderate-to-vigorous-intensity physical activity, abdominal fat accumulation and dysfunction of intra-abdominal adipose tissue remained in a higher degree in early-life exposed women than non-exposed women, which provided clinical evidence which supported previous findings[24]. Therefore, it is warranted to suppose that moderate-to-vigorous-intensity physical activity could modify the risks of central obesity and its related metabolic disorders but not fully adjust these risks. Physical activity could serve as a supplementary intervention for women with high risk of central obesity.

The early-life exposure to famine contributed to an increased risk of central obesity and its related metabolic disorders, of which the mechanism remains unclear. Animal research has found that offspring of undernourished mothers showed lower birth weight but larger proportion of retroperitoneal fat pads to overall weight, which represented visceral fat accumulation, than offspring of well-nourished mothers[26]. The thrifty phenotype hypothesis proposes that poor nutrition in early life produces permanent changes in metabolism, which result in the observed epidemiological associations between poor fetal and infant growth and the subsequent development of the metabolic syndrome[27]. Tobi *et al.* enrolled Dutch participants with prenatal exposure to famine. After evaluation of their whole blood samples, they discovered that along the pathways related to growth and metabolism, the regions of differential methylation extended[28]. Hence, epigenetic plasticity, which may also extend into the postnatal life stage, could explain the mechanism underlying the biological phenomenon that nutritional events early in life were related to metabolic diseases later in life, which is so-called 'metabolic imprinting', to some extent[29]. Bioinformatics studies proposed that malnutrition in the perinatal period could lead to long-lasting change in the expression of gene clusters that regulated insulin signalling and nutrient sensing, and further influence the detection and use of lipid nutrients as fuel[30].

There are some limitations in the present study. Firstly, the present study did not consider other potential confounders, such as birth weight and social status, which might protect women from famine exposure. However, any greater access to food was limited to a very small proportion of the Chinese population due to the egalitarian policy before China's reform, so this might not influence the present study findings significantly. Secondly, the duration and severity of famine varied from region to region. The present study population, however, was restricted to the residents of south-east cities in China. Our findings should be verified and generalised in a larger population in future studies. Thirdly, food restriction or starvation might exert influence on patterns of binge eating and other eating pathologies[31], which contributed to the development of obesity. The change in feeding habits in women with exposure to famine should be taken into consideration in future studies.

In conclusion, early-life exposure to famine is associated with an increased risk of central obesity. Early-life exposure to famine contributed to abdominal fat accumulation and dysfunction, which was independent of the influence of genetic background and lifestyle intervention.

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X. G. and G. C. designed the study. X. H., J. W., W. Y., L. Y., W. P., Q. S., X. C. and Q. L. collected the data. X. H. performed statistical analysis and wrote the paper. X. H., J. W., G. C. and X. G. revised the paper and contributed to discussion.

There are no conflicts of interest.

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