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The association of serum serine levels with the risk of incident cancer: results from a nested case–control study

Tong Liu,†[a,b,c] Chenan Liu,†[a,b,c] Mengmeng Song,†[a,b,c] Yaping Wei,[d] Yun Song,[e] Ping Chen,[e] Lishun Liu,[e] Binyan Wang*[e,f] and Hanping Shi ID *[a,b,c]

Background: Cancer is associated with the dysregulation of serum serine levels, and tumor growth is supported by increased serine biosynthesis. This study aims to explore the association of serum serine levels with incident cancer risk in Chinese hypertensive adults. *Materials and methods*: 1391 patients with incident cancer and 1391 matched controls in terms of age, sex, and residence with cases in a 1 : 1 ratio were included in this nested case–control study. The serum serine concentrations were determined by liquid chromatography with tandem quadrupole mass spectrometry (LC-MS/MS) at the baseline. The associations of serum serine levels with the risk of overall, digestive system, non-digestive system, and lung cancers (the most common type) were assessed by conditional logistic regression. *Results*: When serum serine concentration was assessed as quartiles, a significantly higher risk of total cancer (OR = 1.32; 95% CI: 1.01–1.71; $P = 0.038$) was found in participants in the highest quartile (≥ 17.68 μg mL^{-1}) compared with participants in the lowest quartile (< 13.27 μg mL^{-1}). Similar results were also observed for non-digestive system and lung cancers, but not for digestive system cancers. Significant associations of serum with overall cancer risk were found among all age subgroups, men, non-smokers, non-drinkers, and individuals with lower folic acid levels. *Conclusion*: High serum serine concentrations were associated with an increased risk of overall, non-digestive system, and lung cancers among Chinese hypertensive adult patients.

Introduction

Cancer is a focal clinical and public health issue worldwide. In 2020, in over 185 countries, it was estimated that there were 19.3 million new cancer cases and 10.0 million cancer deaths.[1] According to the Global Cancer Statistics (2002), the top three most frequently diagnosed cancers are as follows: lung cancer, breast cancer, and colorectal cancer.[2] It is estimated that 4.3 million new cases of cancer and 2.8 million cancer deaths occurred in China in 2015.[3] Identifying important and valid

risk factors is urgently needed for curbing the rising trend of cancer. Cancer emergence is associated with a variety of factors including genetics, family history, lifestyle, and microbial infection. Recent studies have found that cancer is also a metabolic disease, which mainly manifests as cell metabolic reprogramming, a hallmark of malignancy.[4] Cancer cells require more nutriment than normal cells, such as glucose, glutamine, and serine, to synthesize the substances necessary to sustain rapid cell growth and proliferation.[5]

In addition to being a non-essential amino acid, serine can be synthesized by cells utilizing their serine synthesis pathway (SSP). Serine plays a critical, pivotal role in intermediary metabolism, and links biosynthetic flux from glycolysis to purine synthesis, glutathione synthesis, folate-mediated one-carbon metabolism, and lipid metabolism.[6] The dysregulation of plasma serine is associated with various diseases, including metabolic syndrome,[7] schizophrenia and major depression,[8,9] cystathionine beta-synthase deficiency,[10] fatty liver,[11] type I diabetes,[12] hypertensive nephrosclerosis,[13] primary biliary cholangitis,[14] and cancer. As the third highest metabolite consumed by cancer cells in nucleotide biosynthesis, serine is also a carbon donor and a building block for proteins.[15] Cancer cells depend on endogenous and exogenous serine to

[a]Department of Gastrointestinal Surgery/Clinical Nutrition, Capital Medical University Affiliated Beijing Shijitan Hospital, Beijing, 100038, China. E-mail: shihp@ccmu.edu.cn
[b]Beijing International Science and Technology Cooperation Base for Cancer Metabolism and Nutrition, Beijing, 100038, China
[c]Key Laboratory of Cancer FSMP for State Market Regulation, Beijing, 100038, China
[d]Key Laboratory of Precision Nutrition and Food Quality, Ministry of Education, Department of Nutrition and Health, College of Food Sciences and Nutritional Engineering, China Agricultural University, Beijing 100083, China
[e]Shenzhen Evergreen Medical Institute, Shenzhen, China. E-mail: binyanwang163@163.com
[f]Institute for Biomedicine, Anhui Medical University, Hefei, China
† These authors contributed equally to this work and share the first author.

enhance their metabolism and proliferation. In addition, studies have found that a decrease in serine biosynthesis leads to an increase in tumor growth in several different cancers.[5,16]

A recent study revealed that serum serine was higher among smokers with bladder cancer compared to non-smokers,[17] and another study found that high levels of serine were associated with decreased overall survival of patients with head and neck cancer.[18] Intriguingly, researchers found that alterations of some free amino acids, such as serine, occur in the serum of non-small-cell lung cancer (NSCLC) patients in the early stage of the disease, and this might serve as a valuable component of a blood multi-marker panel for NSCLC detection.[19] All of these studies indicated that patients with cancer showed dysregulation of serum serine. To date, no study has been conducted to explore the association of serum serine concentrations with subsequent cancer risk. Our study aims to examine the relationship between serum serine concentrations and cancer risk using a case–control study nested in a prospective cohort study.

Materials and methods

Study population and design

The participants for this nested, case–control study were obtained from the China H-Type Hypertension Registry Study (CHHRS; https://www.chictr.org.cn/showproj.html?proj=28262; unique identifier: ChiCTR1800017274). In brief, the CHHRS was a community-based, observational, real-world registry study including 87 492 participants, conducted primarily in Rongcheng city, Shandong Province, China, from July 2018 to July 2023. Participants eligible for the study were men and women over the age of 18 with hypertension systolic blood pressure (SBP) ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and without a history of cancer at the screening visit. In the current study, two phases are involved: recruitment (screening) and a three-year observation follow-up. Follow-ups were scheduled every three months to collect measurement data, and to record blood pressure, medication usage, and

study outcomes, such as cardiovascular disease, cancer, and all-cause mortality.

Outcome ascertainment

From 2016 to 2019, cancer cases were identified based on certain clinical criteria including operative recordings, imaging results, and serum tumor markers or positive histopathology data from hospitals that had treated cancer patients. In the absence of pathological data, two oncologists assessed potential cases. To identify cancer cases, the two professionals had to diagnose it at the same time and code it using the International Classification of Diseases, 10th Revision (ICD-10).

Nested case–control study

As a result of the CHHRS follow-up, 1419 cancer cases were identified among 87 492 participants in the Rongcheng District. Within this cohort, 1419 incident cancer cases and 1419 matched controls were included in a nested case–control study. Participants belonging to the control group were those who were still alive and had not developed cancer during the follow-up, and matched in terms of age, sex, and residence with cases in a 1 : 1 ratio. After excluding those without data on serine and unpaired individuals, 1391 incident cases and 1391 matched controls were analyzed (Fig. 1). Participants were further divided according to the quartiles of serine concentration with the cutoffs 13.27 μg mL^{-1}, 15.27 μg mL^{-1}, and 17.67 μg mL^{-1}, respectively.

The CHHRS and the present study were approved by the ethics committee of the Institute of Biomedicine, Anhui Medical University in Hefei, China, and adhered to the Declaration of Helsinki. Each participant gave written, informed consent before participating in the study.

Exposure and potential confounders

Data on socioeconomic status, lifestyle behaviors, and medical history of the participants and their families were collected using a standard questionnaire.[20] Participants' height, weight, and waist and hip circumference were measured by trained
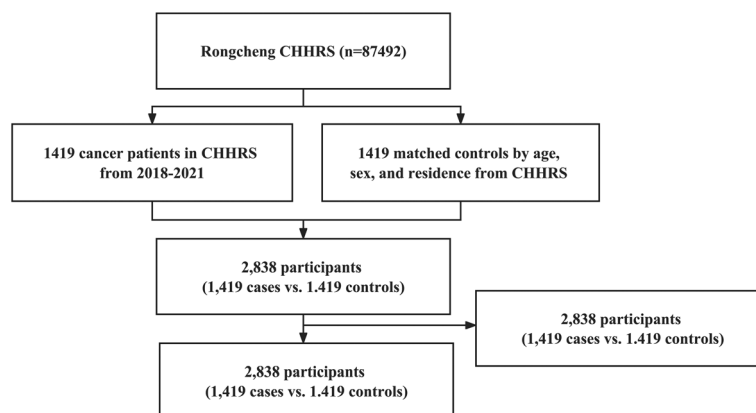

Fig. 1 Flow chart of the study participants in the nested case–control study within the CHHRS.

medical staff. EDTA-containing vacuum tubes were used to collect overnight fasted venous blood samples. Serum folate levels were measured by a commercial laboratory using a chemiluminescent immunoassay (New Industrial, Shenzhen, China). Liquid chromatography with tandem quadrupole mass spectrometry (LC-MS/MS) was used in a commercial laboratory (Beijing DIAN Medical Laboratory, China) to determine serum serine concentrations. At the Shenzhen Tailored Medical Laboratory, serum levels of biochemical indexes including triglycerides (TG), total cholesterol (TC), albumin (ALB), high-density lipoprotein cholesterol (HDL-C), fasting blood glucose (FBG), uric acid (UA), and creatinine were measured using automatic clinical analyzers (Beckman Coulter).

Statistical analysis

Normally distributed variables, skewed distributed variables, and categorical variables were expressed as mean ± standard deviation, median with interquartile range, and n (%), respectively, with the differences between cases and controls compared by paired Student's t-tests, non-parametric Kruskal–Wallis tests, and chi-square tests. Restricted cubic spline regression (RCS) was used to calculate the dose–response association of serine with the risk of overall, digestive system, and non-digestive system cancers. Odds ratios (ORs) of incident cancer in terms of serum serine concentrations (continuous and quartiles) were calculated using conditional logistic regression models. Multivariate regression models were adjusted for body mass index (BMI), smoking status, alcohol consumption, sleep quality, antihypertensive drug usage, SBP (as continuous), FBG (as continuous), TC (as continuous), TG (as continuous), UA (as continuous), creatinine (as continuous), folate (as continuous), alanine aminotransferase (ALT, as continuous), ALB (as continuous), and the family history of cancer.

Age, sex, BMI, smoking and drinking are strongly associated with the risk of cancer development and may influence the role of serum serine with tumor development.[21] Studies have shown that the metabolism of folic acid and the interconversion of serine in the folate cycle may play a role in tumor prevention before precancerous lesions form, and once precancerous lesions are formed, the administration of folate and serine and other nutrients may provide DNA precursors for tumor cell growth to accelerate tumor progression.[22] In further hierarchical analyses, potential interaction effects of the association between serum serine concentrations and cancer risk were assessed by dividing all participants into different subgroups including age (median), sex, BMI, smoking and drinking status, and the levels of folate (median). We further explored the effect of serine on the occurrence of digestive, non-digestive system, and lung cancers (the most common cancer type) by using its cutoffs of quartiles. To avoid any possible influence of preclinical disease on the results, we further divided participants by the median follow-up and reanalyzed the association of serum serine with cancer risk.

A two-tailed $P < 0.05$ was considered statistically significant in all analyses. SAS software (version 9.4) and R software (version 4.0.4, https://www.R-project.org/) were used for all statistical analyses.

Results

Characteristics of the participants

Among the 1391 incident cancer cases, 543 (39.04%) were digestive system cancers and 848 (60.96%) were non-digestive system cancers. Lung cancer was the leading type ($n = 361$), followed by colorectal cancer ($n = 180$), gastric cancer ($n = 160$), liver cancer ($n = 107$), breast cancer ($n = 86$), and other types of cancer ($n = 497$). The mean age of all participants was 69.30 years (SD, 7.77 years). Significant differences were found in the levels of ALB, TC, serine, the percentage of the smoking status, the history of coronary heart disease, the history of stroke, sleep quality, and antihypertensive drug usage across the two groups (all $p < 0.05$, Table 1).

Association of serum serine concentration with cancer risk

The median follow-up in this current study was 0.85 (0.41, 1.21) years. According to the restricted cubic spline graph, serum serine concentration was positively associated with overall, the digestive system and non-digestive system cancer risk (Fig. 2).

Consistently, when serum serine concentration was assessed as a continuous variable, each standard deviation (SD) increment of serum serine levels significantly elevated the risk of overall cancer (OR = 1.12; 95% CI: 1.02–1.23) in the adjusted model (Table 2). When serum serine concentrations were assessed as quartiles, a significantly higher risk of total cancer was found in the participants in the highest quartile (≥ 17.68 μg mL^{-1}) compared with the participants in the lowest quartile (<13.27 μg mL^{-1}) (OR = 1.32; 95% CI: 1.01–1.71; $P = 0.038$). Similar results were also observed for non-digestive system and lung cancers, but not for digestive system cancers (Table 3). A higher risk of non-digestive system cancers (OR = 1.29; 95% CI: 1.01–1.82) and lung cancers (OR = 1.61; 95% CI: 1.03–2.88) was found in participants in the highest vs. the lowest quartiles of serum serine.

Subgroup analyses stratified by confounders and follow-up time

Various subgroup analyses were performed to determine whether serum serine concentrations were associated with total cancer risk (Fig. 3). Age, sex, BMI, smoking status, drinking status, and the levels of folate did not modify the association between serine concentrations and the risk of overall cancer (all p for interaction >0.05). Significant associations of serum serine with overall cancer risk were found among all age subgroups, men, non-smokers, non-drinkers, and individuals with lower folic acid levels. Table 4 shows the association of serine with the overall cancer risk stratified by the median follow-up. Elevated concentrations of serum serine were associated with an increased risk of overall cancer that occurred before the median follow-up (per SD increment, OR = 1.16;

Table 1 Baseline characteristics of the cases and matched controls

| Variables	Controls ($n = 1391$)	Cases ($n = 1391$)	p-Value
Age, years	69.30 ± 7.77	69.30 ± 7.77	0.999
Male, n (%)	779 (56.00)	779 (56.00)	1.000
BMI, kg m^{-2}	25.73 ± 3.60	25.73 ± 3.83	0.950
Baseline SBP, mmHg	148.48 ± 21.25	147.51 ± 21.30	0.934
Baseline DBP, mmHg	83.74 ± 11.32	83.07 ± 11.75	0.129
ALT, U L^{-1}	10.0 (7.0, 13.0)	10.0 (7.0, 14.0)	0.140
ALB, g L^{-1}	45.44 ± 2.45	44.75 ± 2.97	<0.001
TG, mmol L^{-1}	1.21 (0.86, 1.77)	1.19 (0.84, 1.80)	0.641
TC, mmol L^{-1}	6.51 ± 1.23	6.44 ± 1.30	0.045
UA, µmol L^{-1}	320.0 (269.0, 371.0)	314.0 (264.0, 374.0)	0.389
HDL-C, mmol L^{-1}	1.23 ± 0.24	1.22 ± 0.27	0.243
FBG, mmol L^{-1}	6.25 ± 1.71	6.29 ± 1.83	0.613
Creatinine, µmol L^{-1}	51.0 (10.0, 64.0)	52.0 (10.0, 64.0)	0.752
Folate, ng ml^{-1}	6.14 (3.99, 9.68)	6.12 (4.23, 10.13)	0.450
HCY, µmol L^{-1}	12.01 (10.31,14.66)	12.25 (10.06, 15.03)	0.904
Serine, µg mL^{-1}	15.16 (13.11,17.47)	15.37 (13.41,17.82)	0.001
Marital status, n (%)	1146 (82.39)	1180 (84.83)	0.354
Educational background, n (%)	109 (7.84)	103 (7.40)	0.668
Current smoker, n (%)	334 (24.01)	401 (28.83)	0.011
Current drinker, n (%)	388 (27.89)	370 (26.60)	0.359
History of CKD, n (%)	14 (1.01)	25 (1.80)	0.076
History of CHD, n (%)	0 (0)	165 (11.86)	<0.001
History of stroke, n (%)	0 (0)	64 (4.60)	<0.001
Family history of cancer, n (%)	47 (3.38)	50 (3.59)	0.918
Sleep quality, n (%)	191 (13.73)	259 (18.62)	0.002
Antihypertensive drug usage, n (%)	495 (35.59)	557 (40.04)	0.015

BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; ALT: alanine aminotransferase; ALB: albumin; TG: triglycerides; TC: total cholesterol; UA: uric acid; HDL-C: high-density lipoprotein cholesterol; FBG: fasting blood glucose; HCY: homocysteine; CKD: chronic kidney disease; CHD: coronary heart disease.

95% CI: 1.02–1.33; $P = 0.025$) and after the median follow-up (Q4 *vs.* Q1; OR = 1.37; 95% CI: 1.01–1.95; $P = 0.048$), when serine was assessed as continuous and quartiles, respectively.

Discussion

In this case–control study, nested in a prospective cohort population of the CHHRS, we found that hypertensive adults with elevated serum serine concentrations were associated with an increased risk of overall, non-digestive system and lung cancers. The results remained stable even after stratifying participants by age, sex, smoking status, drinking status, levels of folic acid, and follow-up time.

This is the first study to reveal an association between serum serine concentrations and the incident risk of cancer in a population with hypertension. Cadoni *et al.* reported that a high level of serum serine was associated with decreased overall survival of head and neck cancer (HNC) patients (hazard ratio, HR = 2.71, 95% CI: 1.39–5.31),[18] but was not associated with an increased risk of advanced stage HNC (OR: 1.76, 95% CI: 0.95–3.26). However, the authors did not report on the distribution of serum serine in participants with or without cancer, nor on the association of serum serine with incident cancer risk. Two studies revealed that serum serine is a potential biomarker of colorectal cancer (CRC) (area under curve, AUC = 0.81) and NSCLC (AUC = 0.993), differentiating cancer patients from healthy controls.[23,24] However, both studies only reported that serum serine levels were decreased in cancer patients, and did not explore the association of serum serine with incident cancer risk. Conversely, a recent study reported that serum serine concentrations were higher in CRC and colorectal polyp patients than in healthy controls,[25] and indicated that abnormal changes in serine metabolism may be an important reason for CRC progression. Notably, a previous study[19] reported that some of the free amino acid alterations occurred in the serum of NSCLC patients in the early stage of the disease, and 6 amino acids (including serine) could be used as a blood multi-marker
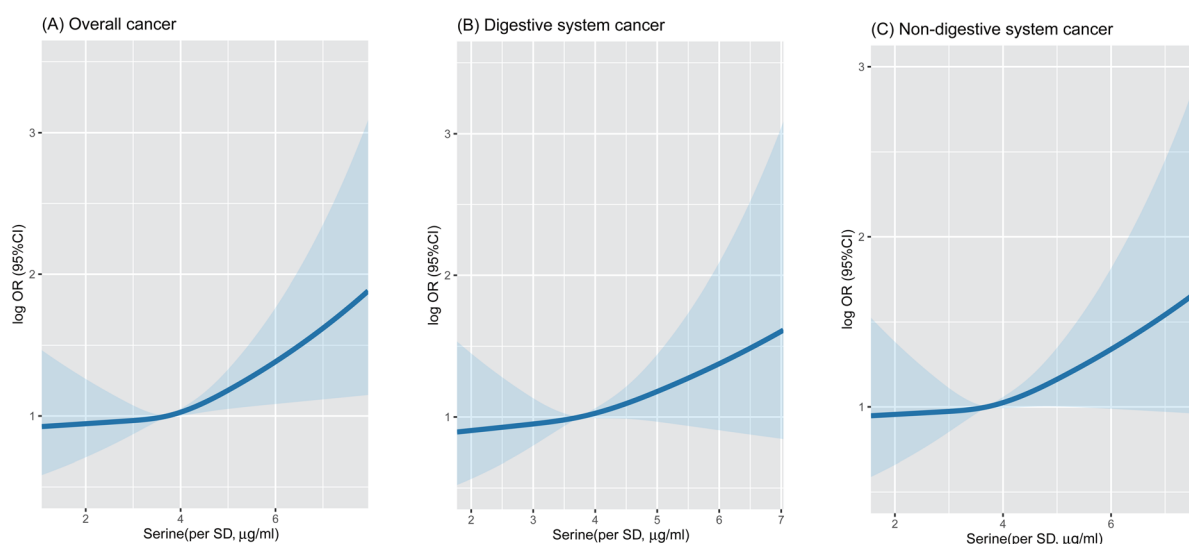
Fig. 2 Association between serum serine concentrations and cancer risk using RCS. Note: models were adjusted for body mass index, smoking status, alcohol drinking, systolic blood pressure, triglycerides, cholesterol, uric acid, fasting blood glucose, high-density lipoprotein cholesterol, creatinine, albumin, alanine aminotransferase, homocysteine, sleep quality, antihypertensive drug usage, and family history of cancer.

Table 2 The association of serine with overall cancer risk

Serine (μg mL^{-1})	Cases/controls (ratio 1 : 1)	Crude model		Adjusted model	
		OR (95% CI)	p-Value	OR (95% CI)	p-Value
Serine (per SD)	1391/1391	**1.11 (1.03, 1.21)**	**0.011**	**1.12 (1.02, 1.23)**	**0.014**
Quartiles of serine (μg mL^{-1})					
Q1 (<13.27)	322/374	Ref.		Ref.	
Q2 (13.27–15.27)	354/340	1.23 (0.99, 1.53)	0.062	1.14 (0.90, 1.45)	0.284
Q3 (15.28–17.67)	349/348	1.20 (0.96, 1.50)	0.102	1.10 (0.86, 1.41)	0.455
Q4 (≥17.68)	366/329	1.33 (1.06, 1.68)	0.015	1.32 (1.01, 1.71)	0.038

Models were adjusted for body mass index, smoking status, alcohol drinking, systolic blood pressure, triglycerides, cholesterol, uric acid, fasting blood glucose, high-density lipoprotein cholesterol, creatinine, albumin, alanine aminotransferase, homocysteine, sleep quality, antihypertensive drug usage, and family history of cancer.

Table 3 The association of serine with the digestive, non-digestive system and lung cancer risk

Serine	Digestive system cancer[a]		Non-digestive system cancer[b]		Lung cancer[c]	
	Cases/controls	OR (95% CI)	Cases/controls	OR (95% CI)	Cases/controls	OR (95% CI)
Serine (per SD)	543/543	1.13 (0.96, 1.32)	848/848	**1.12 (1.02, 1.26)**	361/361	1.17 (0.97, 1.42)
Quartiles						
Q1	124/148	Ref.	198/226	Ref.	84/96	Ref.
Q2	139/132	1.15 (0.78, 1.71)	214/210	1.11 (0.81, 1.52)	92/86	1.43 (0.84, 2.44)
Q3	136/135	1.16 (0.76, 1.76)	214/209	1.12 (0.81, 1.53)	91/92	1.19 (0.73, 1.96)
Q4	144/128	1.33 (0.87, 2.03)	222/203	**1.29 (1.01, 1.82)**	94/87	**1.61 (1.03, 2.88)**

Models were adjusted for body mass index, smoking status, alcohol drinking, systolic blood pressure, triglycerides, cholesterol, uric acid, fasting blood glucose, high-density lipoprotein cholesterol, creatinine, albumin, alanine aminotransferase, homocysteine, sleep quality, antihypertensive drug usage, and family history of cancer. [a] The cutoffs of serine in digestive system cancer were 13.28, 15.41, and 17.72. [b] The cutoffs of serine in non-digestive system cancer were 13.26, 15.21, and 17.65. [c] The cutoffs of serine in lung cancer were 13.57, 15.44, and 17.82.

panel for NSCLC detection. However, the results were based on the serum amino acid levels in patients with stage I lung cancer, which only represents the detectability of serum serine combined with other amino acids at the early stage of lung cancer, but cannot predict the risk of incident cancer. Our study illustrated that the level of baseline serum serine was higher for cancer cases than for those without cancer. This signifies that an inchoate serum serine fluctuation indicates a higher risk of cancer. Overall, our study revealed the importance of detecting emergent serum serine fluctuations for predicting cancer risk. Additionally, we found more pronounced positive associations between high serum serine levels and cancer risk in participants who were male, non-smokers, non-drinkers, or had lower folate levels, but the interaction tests for these factors and serum serine were not significant.

The biological mechanism by which serine affects cancer risk is not clear. Serine, a pivotal component of one-carbon metabolism,[5] plays an essential role in carbon unit donation and DNA methylation.[26] According to genetic and functional evidence, oncogenesis is driven by hyperactivation of the serine biosynthetic pathway. De novo serine biosynthesis was first observed in tumors in 1955.[27] Snell et al. demonstrated that serine biosynthesis increases during tumor progression.[28] The mechanisms of increased serine synthesis include the overexpression of phosphoglycerate dehydrogenase (PHGDH) in cancer cells,[29,30] which is a key enzyme of the serine synthesis pathway. Additionally, peripheral axons secrete amino
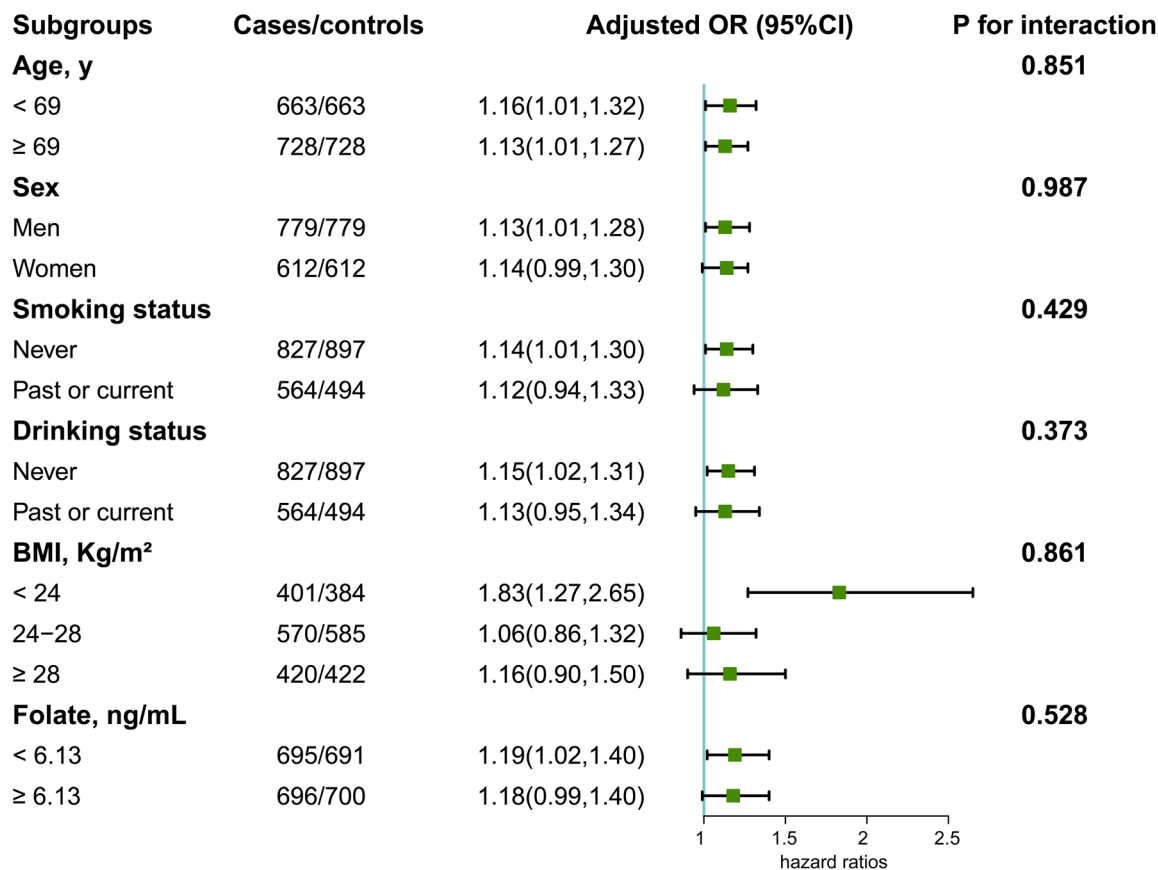
acids, such as serine, to support the growth and proliferation of pancreatic ductal adenocarcinoma.[31] Given the detrimental consequences of increased serine on tumor progression, several studies have attempted to suppress tumor growth by depleting serine or inhibiting the serine synthesis pathway.[32,33] As expected, tumor progression can be restrained by these methods. Whether the beginning of abnormal fluctuation in serum serine concentrations occurs before cancer diagnosis remains unclear. Our study revealed that serum serine dysregulation may signify the emergence of inconspicuous precancerous lesions, which is important for cancer screening and prevention.

A novel aspect of our study is that it examines the association of serum serine levels, a component of one-carbon metabolism, with the risk of cancer in hypertensive adults. Hypertensive patients should be monitored for inchoate serum serine concentrations. Furthermore, it has the advantage of being a nested, case–control study that was derived from a large, prospective cohort study, thus avoiding recall bias. In addition, to eliminate the possibility of a causal association between participants' serum serine concentrations and their cancer diagnosis, baseline blood samples from participants were obtained before any cancer diagnosis could be made.

Several limitations also exist in this study. First, only data of baseline serum serine levels were collected from study participants. It would have been informative to measure serum

Subgroups	Cases/controls	Adjusted OR (95%CI)	P for interaction
Age, y			**0.851**
< 69	663/663	1.16(1.01,1.32)	
≥ 69	728/728	1.13(1.01,1.27)	
Sex			**0.987**
Men	779/779	1.13(1.01,1.28)	
Women	612/612	1.14(0.99,1.30)	
Smoking status			**0.429**
Never	827/897	1.14(1.01,1.30)	
Past or current	564/494	1.12(0.94,1.33)	
Drinking status			**0.373**
Never	827/897	1.15(1.02,1.31)	
Past or current	564/494	1.13(0.95,1.34)	
BMI, Kg/m²			**0.861**
< 24	401/384	1.83(1.27,2.65)	
24−28	570/585	1.06(0.86,1.32)	
≥ 28	420/422	1.16(0.90,1.50)	
Folate, ng/mL			**0.528**
< 6.13	695/691	1.19(1.02,1.40)	
≥ 6.13	696/700	1.18(0.99,1.40)	

hazard ratios

Fig. 3 Stratified analysis of the association of serum serine (per SD) with the risk of overall cancer. Note: models were adjusted for body mass index, smoking status, alcohol drinking, systolic blood pressure, triglycerides, cholesterol, uric acid, fasting blood glucose, high-density lipoprotein cholesterol, creatinine, albumin, alanine aminotransferase, homocysteine, sleep quality, antihypertensive drug usage, and family history of cancer.

Table 4 The association of serine with overall cancer risk stratified by the median follow-up

Serine (µg mL⁻¹)	Cases/controls (ratio 1 : 1)	Before the median follow-up		Cases/controls (ratio 1 : 1)	After the median follow-up	
		OR (95% CI)	p-Value		OR (95% CI)	p-Value
Serine (per SD)	699/699	**1.16 (1.02, 1.33)**	0.025	692/692	1.10 (0.98, 1.26)	0.110
Quartiles of serine						
Q1 (<13.27)	156/186	Ref.		166/188	Ref.	
Q2 (13.27–15.27)	183/165	1.22 (0.86, 1.72)	0.266	171/175	1.15 (0.81, 1.64)	0.436
Q3 (15.28–17.67)	172/181	1.16 (0.81, 1.65)	0.429	177/167	1.17 (0.82, 1.67)	0.374
Q4 (≥17.68)	188/167	1.35 (0.92, 1.97)	0.125	178/162	**1.37 (1.01, 1.95)**	0.048

Models were adjusted for body mass index, smoking status, alcohol drinking, systolic blood pressure, triglycerides, cholesterol, uric acid, fasting blood glucose, high-density lipoprotein cholesterol, creatinine, albumin, alanine aminotransferase, homocysteine, sleep quality, antihypertensive drug usage, and family history of cancer.

serine levels regularly to investigate the dynamic relationship between serum serine levels and cancer risk. Second, the small sample size of incident cancer cases and short follow-up time limited any further analysis of different subtypes of cancer; a larger population with longer follow-up is required to validate the results. Third, the findings of this study cannot be extrapolated to individuals without hypertension because it was conducted in hypertensive adults. However, it

is important to note that the results of the study were not substantially altered after adjusting for blood pressure measurements at the baseline. It is important to emphasize that this study was a preliminary exploration of the association between one-carbon metabolism components and incident cancer risk. These findings warrant the need for future subsequent studies, including large-scale cohort studies and randomized trials.

Conclusions

This study provides the first prospective evaluation of the independent effect of serum serine concentrations on cancer incidence in a hypertensive adult population. There was a significant increase in the risk of cancer in patients with high serum serine levels. The findings may have clinical and scientific significance in cancer prevention. To confirm these findings in other populations, further studies are needed.

Author contributions

Tong Liu: methodology, software, and writing – original draft. Chenan Liu: writing – original draft. Mengmeng Song: methodology and software. Yaping Wei: supervision and validation. Yun Song: investigation and visualization. Ping Chen: supervision. Lishun Liu: supervision and validation. Binyan Wang: validation and supervision. Hanping Shi: conceptualization, supervision, validation, resources and project administration.

Data availability

Data will be made available upon reasonable request.

Ethics approval and consent to participate

The CHHRS and the present study were approved by the ethics committee of the Institute of Biomedicine, Anhui Medical University in Hefei, China, and adhered to the Declaration of Helsinki. Each participant gave written, informed consent before participating in the study.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

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