

# Correlation Study of Branched-Chain Amino Acids in the Diet of Chinese Community old adults and Diabetes

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**Abstract** Objective: Although there was a substantial body of research on the association between branched-chain amino acids (BCAAs) and diabetes, studies focusing on BCAA levels in relation to diabetes in the elderly population are scarce. This study aims to explore the correlation between BCAA levels and diabetes among community-dwelling older adults in China. Methods: Based on the health management cohort project for the elderly in Nanshan District, Shenzhen City, a multistage stratified sampling method was employed from May 2018 to December 2019 to select 4,278 elderly individuals over the age of 65 as the subjects of the study. Validated semi-quantitative food frequency questionnaires, as well as anthropometric and physical performance measurements, were used to collect data. Binary Logistic regression analysis was applied to examine the relationship between dietary branched-chain amino acids (isoleucine, leucine, and valine) and diabetes in the elderly. Results: A total of 4,278 elderly individuals aged 65 and above were included in this study, with an average age of  $72.73 \pm 5.49$  years, of which 1,861 (43.50%) were male. After adjusting for confounding factors, isoleucine remained a risk factor for diabetes (OR=3.575, 95%CI:1.321,10.692), while leucine was a protective factor (OR=0.540, 95%CI:0.357,0.817); these relationships persisted after adjusting for covariates such as age, education level, BMI, etc.; no significant association was observed between valine and diabetes comorbidity. Conclusion: There is a potential correlation between certain branched-chain amino acids, such as isoleucine and leucine, that could serve as risk markers for diabetes in the elderly population.

**Keywords:** Dietary Branched-Chain Amino Acids, Elderly, Diabetes, Isoleucine, Leucine

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## 1. Introduction

With the intensification of the global aging trend, the incidence of chronic diseases among the elderly is rising year by year, imposing a significant burden on society and families. In China, the prevalence of diabetes among the elderly population is continuously increasing, becoming one of the major chronic diseases affecting the health of the elderly. [1] Diabetes not only severely affects the quality of life of patients but also places a heavy burden on the healthcare system. Therefore, in-depth research on the pathogenesis and prevention strategies of diabetes is of great importance for improving the health status of the elderly population.

In recent years, the role of dietary factors in the occurrence of diabetes had increasingly gained attention. Branched-chain amino acids (BCAAs), including leucine,

isoleucine, and valine, are essential amino acids that account for about 40% of the total amino acid requirements of the human body. They play a crucial role in protein metabolism and cell growth. BCAAs cannot be synthesized in the human body and must be obtained through external intake, which is vital for maintaining normal physiological functions. [2,3,4] The relationship between BCAAs and metabolic diseases, especially type 2 diabetes, has attracted widespread attention. Studies have found that disturbances in plasma BCAA metabolism are associated with increased risk of insulin resistance and diabetes. [5,6] Additionally, BCAA levels in the elderly population are significantly higher than in younger individuals. [7] Abnormally elevated levels of BCAAs may lead to mitochondrial dysfunction, inflammatory responses, and lipid metabolism imbalances, thereby affecting insulin signal transduction. [4,8]

The dietary structure of elderly people in China was diverse and influenced by various factors such as

geography, culture, and lifestyle habits. [9,10,11] BCAAs are mainly derived from animal-based foods like meat, eggs, and dairy products. With the improvement of living standards, the intake of animal-based foods among the elderly has increased. However, whether the intake of the elderly dietary BCAAs is appropriate and the specific association with the risk of diabetes still needs further research. Given the potential role of BCAAs in the occurrence of diabetes and the particularity of the dietary structure of elderly people in China, conducting research on the correlation between dietary BCAAs and diabetes among community-dwelling elderly in China holds significant value. This study aimed to explore the relationship between the intake level of dietary BCAAs in the elderly and the risk of developing diabetes, assessed the potential impact of BCAA metabolism on the prevention and treatment of diabetes, and provided a scientific basis for formulating appropriate dietary guidance and intervention strategies.

## 2. Material and Methods

### 2.1. Study Design

The data utilized in this study were derived from the Nanshan District Elderly Population Cohort, a cross-sectional study on the population established based on the national community elderly residents' free health check-up project in China, aimed at investigating the nutrition and health status of adults aged 65 and above in China. The data collection was conducted from May 2018 to December 2019 across 53 community health service centers in 8 blocks of Nanshan District, Shenzhen City, China, using a stratified cluster random sampling method. Initially, a total of 4,478 elderly individuals were enrolled in the baseline study. The study established inclusion and exclusion criteria, admitting participants who met the following conditions: (i) aged 65 or above; (ii) residing in Shenzhen for at least six months; (iii) undergoing annual health check-ups at community health service centers; (iv) voluntarily participating and capable of completing the survey, and signing an informed consent form. Participants were excluded if they met any of the following conditions: (i) under the age of 65 (n=3); (ii) refusing to participate in the questionnaire survey (n=6); (iii) lacking dietary records or disease history reports, and those with implausible dietary energy intake (<600 kcal/day or >4000 kcal/day) (n=191).

Ultimately, a total of 4,278 eligible participants were included in the analysis. Written consent was obtained from all participants, and the study protocol was approved by the Ethics Committee of the Chronic Disease Prevention and Control Center of Nanshan District, Shenzhen City (No.1120180009), with informed consent obtained from the research subjects.

### 2.2. Dietary Assessment

This study used a validated food frequency questionnaire (FFQ) [12] to assess habitual dietary consumption, which was based on food intake in the month before the interview. Due to differences in eating

habits, some infrequently eaten foods were not included. A total of 62 food items were listed in the semi-quantitative 81-item FFQ, which had previously been validated using six 3-day energy-adjusted diet records of 26 nutrients among Guangzhou women. [12] Each food item (serving sizes such as bowls, boxes, cups, grams, etc.) was assigned a common unit or portion size, and participants were asked to report their average food consumption across four frequency categories (never, monthly, weekly, and daily). Color photographs of portion sizes of the corresponding foods were provided during follow-up to assist in quantifying food portions. The consumption of each food item was converted to daily intake (g/d), and daily nutrient intake was estimated based on the "Chinese Food Composition Table" (2019 edition). [13] The total intake of branched-chain amino acids was calculated as the cumulative sum of the three amino acids (leucine, isoleucine, and valine).

### 2.3. Data Collection

This study primarily collected data through questionnaire surveys, physical measurements, and laboratory examination. Each community health service center established a survey team consisting of three members. The questionnaire survey was conducted by community healthcare personnel through one-on-one face-to-face interviews, utilizing a tablet-based visual questionnaire system equipped with real-time recording and intelligent logic checks. Prior to the survey, trained nursing staff read the informed consent form to the participants, explaining the purpose, significance, specific examination items, and potential risk factors associated with the project, and obtained signed consent based on the participants' willingness.

- (1). Questionnaire Survey: The survey gathered information on key demographic characteristics (gender, age, education level, marital status, BMI, etc.), lifestyle behaviors (physical exercise, sleep patterns, smoking, alcohol consumption, regular night shifts in youth, etc.), and diabetes, it assessed the frequency of food intake over the past month.
- (2). Physical Measurements: Measurements included weight, height, waist circumference, and blood pressure.
- (3). Laboratory examination: All participants provided fasting venous blood samples in the morning, with a minimum fasting period of 8 hours prior to sampling. Blood samples were analyzed using an automated biochemical analyzer (HITACHI 7080). The tests included lipid metabolism biomarkers such as total cholesterol (TC), total triglycerides (TG), high-density and low-density lipoprotein (HDL-C and LDL-C) and so on.

### 2.4. Outcome Indicators and Related Definitions

Diabetes: [14] According to the diagnostic criteria of the Diabetes Branch of the Chinese Medical Association, diabetes is diagnosed when the fasting blood glucose level is  $\geq 7.0$ mmol/L; the random blood glucose level is  $\geq 11.1$ mmol/L and is accompanied by obvious diabetes

symptoms; the 2-hour blood glucose level of the glucose tolerance test is  $\geq 11.1$ mmol/L; or the glycated hemoglobin level is  $\geq 6.5$ %. Participants in the survey who are actively undergoing medication therapy for diabetes.

Physical activity: [15] The International Physical Activity Questionnaire (IPAQ) calculates the level of physical activity at a certain intensity per week: the MET assignment corresponds to physical activity  $\times$  weekly frequency (d/w)  $\times$  daily time (min/d), and divides physical activity into three levels: low-, medium-, and high-intensity exercise.

## 2.5. Statistical Analysis

An Epidata database was used for data management, and variables with less than 5% data missing were interpolated using a multiple-interpolation method. The SPSS 26.0 software was used for data analysis. If the two-tailed  $P < 0.05$ , the difference was considered statistically significant.

For quantitative data that did not follow a normal distribution, median (interquartile range) was used for description, and the Wilcoxon rank-sum test was employed for comparisons between two groups. Categorical data were described using frequency or proportion (%), with the chi-square test used for group comparisons. The dietary intake of branched-chain amino acids (BCAAs) was categorized into tertiles (Q1-Q3).

Firstly, differences in the characteristics of the participants were explored according to the coexistence of MCCs and the BCAA quintiles. Binary logistic regression was utilized to analyze the association between the three amino acids (isoleucine, leucine, and valine) and diabetes. Model 1 was unadjusted for any confounding factors, Model 2 adjusted for gender and age, and Model 3 further adjusted for smoking and drinking status, BMI, physical activity level, education level, and household registration.

## 3. Result

### 3.1. Basic CHAracteristics of the Participants

A flow chart of the participant recruitment process is shown in Figure 1 and the basic characteristics of the participants are shown in Table 1. Among the 4,278 participants, there were 1,861 males (43.50%), with an average age of  $72.73 \pm 5.49$  years. Significant differences were observed between males and females in terms of age, marital status, education level, regular night shift work, smoking, alcohol consumption, sleep duration, and central obesity ( $P < 0.05$ ). However, no statistically significant differences were found between males and females regarding household registration, physical activity level, BMI categories, blood pressure, total cholesterol, triglycerides, high-density lipoprotein, and low-density lipoprotein ( $P > 0.05$ ).

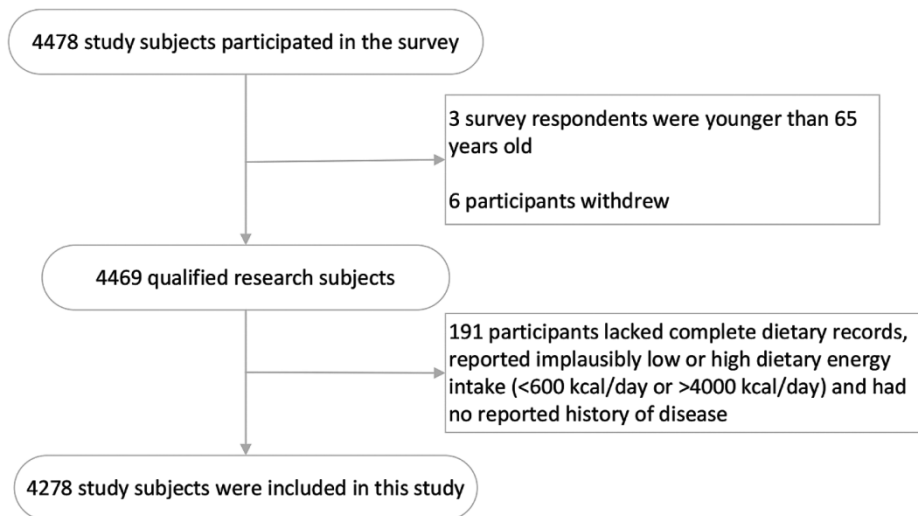


Figure 1. A flow chart of the participant recruitment process

Table 1. Basic Characteristics Of The Research Object [n (%)]

Characteristics	Total (N= 4278)	Male (n1=1861)	Female (n2=2417)	P-value
Age				< 0.001
65~69	1469(34.3)	560(30.1)	909(37.6)	
70~74	1472(34.4)	651(35.0)	821(34.0)	
75~79	731( 17.1)	335(18.0)	396(16.4)	
$\geq 80$	606(14.2)	315(16.9)	291(12.0)	
Marital status				< 0.001
Married/common-law marriage	3379(79.0)	1730(93.0)	1649(68.2)	
Divorce/widowhood/Unmarried	899(21.0)	131(7.0)	768(31.8)	
Education level				< 0.001
Primary school and below	1243(29.0)	366(19.7)	877(36.3)	
Junior / High School	1594(37.3)	719(38.6)	875(36.2)	

Characteristics	Total (N= 4278)	Male (n1=1861)	Female (n2=2417)	P-value
Secondary school and above	1441(33.7)	776(41.7)	665(27.5)	
Place of domicile				0.238
City	2563(59.9)	1107(59.5)	1456(60.2)	
Town	469(11.0)	221(11.9)	248(10.3)	
Rural district	1246(29.1)	533(28.6)	713(29.5)	
Whether regular night shift				0.001
Yes	920(21.5)	445(23.9)	475(19.7)	
No	3358(78.5)	1416(76.1)	1942(80.3)	
Intensity of exercise				0.336
low intensity	805(18.8)	333(17.9)	472(19.5)	
moderate strength	2838(66.4)	1242(66.7)	1596(66.0)	
high intensity	635(14.8)	286(15.4)	349(14.5)	
Sleep times ( hours )				< 0.001
<6	977(22.8)	295(15.9)	682(28.2)	
6~8	2879(67.3)	1332(71.5)	1547(64.0)	
>8	422(9.9)	234(12.6)	188(7.8)	
Smoke status				< 0.001
Never	3383(79.1)	988(53.1)	2395(99.1)	
Former	508 (11.9)	496(26.7)	12(0.5)	
Current	387(9.0)	377(20.3)	10(0.4)	
Drinking status				< 0.001
Never	3553(83.1)	1249(67.1)	2304(95.3)	
Former	147(3.4)	106(27.2)	41(1.7)	
Current	578(13.5)	506(5.7)	72(3.0)	
Abdominal Obesity				< 0.001
Yes	1765(41.3)	551(29.6)	1214(50.2)	
No	2513(58.7)	1310(70.4)	1203(49.8)	
SBP(mmHg)*	133(124, 141)	133(124, 142)	131(124, 141)	0.554
DBP(mmHg)*	75(70,81)	75(70,81)	75(70,81)	0.201
BMI*	24.07(22.42,25.79)	24.07(22.56,25.83)	24.07(22.32,25.73)	0.073
GLU(mmol/L)*	5.22(4.87,5.83)	5.22(4.88,5.87)	5.22(4.86,5.77)	0.059
TC(mmol/l)*	5.14(4.54,5.75)	5.14(4.52,5.68)	5.14(4.57,5.79)	0.068
TG(mmol/L)*	1.32(1.03,1.75)	1.32(1.05,1.75)	1.32(1.03,1.76)	0.651
HDL(mmol/L)*	1.35(1.20, 1.54)	1.35(1.20, 1.54)	1.35(1.21, 1.55)	0.125
LDL(mmol/L)*	2.97(2.51,3.44)	2.97(2.52,3.42)	2.97(2.51,3.45)	0.365

Note : \* is skewed distribution, expressed by M ( Q1, Q3 ).

**Table 2. Basic Distribution Of Total Dietary Branched-chain Amino Acids [Case (%)]**

Characteristics	Q1	Q2	Q3	P-value
Sexa				< 0.001
Male	508(35.6)	618(53.3)	735(51.5)	
Female	918(64.4)	808(56.7)	691(48.5)	
Agea				0.002
65~69	514(36.0)	495(34.7)	460(32.3)	
70~74	517(36.3)	460(32.3)	495(34.7)	
75~79	232(16.3)	260(18.2)	239(16.7)	
≥80	163(11.4)	211(14.8)	232(16.3)	
Marital status				< 0.001
Married/common-law marriage	1059(74.3)	1124(78.8)	1196(83.9)	
Divorce/widowhood/Unmarried	367(25.7)	302(21.2)	230(16.1)	
Education level				< 0.001
Primary school and below	566(39.7)	397(27.8)	280(19.6)	
Junior / High School	536(37.6)	520(36.5)	538(37.7)	
Secondary school and above	324(22.7)	509(35.7)	608(42.7)	
Place of domicile				< 0.001
City	691(48.5)	869(60.9)	1003(70.3)	
Town	199(14.0)	142(10.0)	128(9.0)	
Rural district	536(37.5)	415(29.1)	295(20.7)	
Intensity of exercise				< 0.001
low intensity	317(22.2)	261(18.3)	227(15.9)	

Characteristics	Q1	Q2	Q3	P-value
moderate strength	942(66.1)	962(67.5)	934(65.5)	
high intensity	167(11.7)	203(14.2)	265(18.6)	
Sleep times ( hours )				0.275
<6	335(23.5)	325(22.8)	317(22.2)	
6~8	939(65.8)	954(66.9)	986(69.1)	
>8	152(10.7)	147(10.3)	123(8.7)	
Smoke status				0.010
Never	1158(81.3)	1121(78.6)	1104(77.4)	
Former	149(10.4)	159(11.2)	200(14.0)	
Current	119(8.3)	146(10.2)	122(8.6)	
Drinking statusa				0.001
Never	1227(86.0)	1183(83.0)	1143(32.2)	
Former	156(10.9)	196(13.7)	226(15.8)	
Current	43(3.0)	47(3.3)	57(4.0)	
Abdominal Obesitya				0.003
Yes	632(44.3)	591(41.4)	542(38.0)	
No	794(55.7)	835(58.6)	884(62.0)	
Diabetes				0.939
Yes	341(23.9)	344(24.1)	349(24.5)	
No	1085(76.1)	1082(75.9)	1077(75.5)	

Note : The truncation values of the BCAAs quantile are as follows: Q1: Q1<9.416g/day, Q2: 9.416g/day~13.537g/day, Q3:  $\geq$ 15.537g/day.

**Table 3. General Demographic Characteristics Of Diabetes Mellitus In The Elderly**

Characteristics	Total (N= 4278)	Diabetes		P-value
		Yes	No	
Diabetes				0.081
Yes	1861	474(45.8)	1387(42.8)	
No	2417	560(54.2)	1857(57.2)	
Age				< 0.001
65~69	1469	290(28.1)	1179(36.3)	
70~74	1472	368(35.6)	1104(34.0)	
75~79	731	208(20.1)	523(16.2)	
$\geq$ 80	606	168(16.2)	438(13.5)	
Place of domicile				0.034
City	2563	652(63.1)	1911(58.9)	
Town	469	113(10.9)	356(11.0)	
Rural district	1246	269(26.0)	977(30.1)	
Marital status				0.180
Married/common-law marriage	3379	832(80.5)	2547(78.5)	
Divorce/widowhood/Unmarried	899	202(19.5)	697(21.5)	
Education level				0.004
Primary school and below	1243	263(25.5)	980(30.2)	
Junior / High School	1594	386(37.3)	1208(37.2)	
Secondary school and above	1441	385(37.2)	1056(32.6)	
Intensity of exercise				0.271
low intensity	805	178(17.2)	627(19.3)	
moderate strength	2838	705(68.2)	2133(65.8)	
high intensity	635	151(14.6)	484(14.9)	
Sleep times ( hours )				0.235
<6	977	236(22.8)	741(22.8)	
6~8	2879	682(66.0)	2197(67.8)	
>8	422	116(11.2)	306(9.4)	
Smoke status				0.100
Never	3383	803(77.7)	2580(79.5)	
Former	508	142(13.7)	366(11.3)	
Current	387	89(8.6)	298(9.2)	
Drinking status				0.218
Never	3553	869(84.0)	2684(82.7)	
Former	578	138(13.4)	440(13.6)	
Current	147	27 ( 2.6 )	120(3.7)	

### 3.2. Distribution of Dietary Total Branched-Chain Amino Acids in the Elderly Population

The dietary intake of branched-chain amino acids (BCAAs) was categorized into tertiles. Individuals with higher BCAA intake (Q3) were more likely to be male, aged 75 to 79, married, have a higher level of education, reside in urban areas, engage in high-intensity physical activity, be non-central obese, and have never smoked or consumed alcohol compared to those with lower intake (Q1).

### 3.3. General Population Characteristics of the Elderly

Table 3 indicated that the prevalence of diabetes among the elderly was associated with increasing age, urban residency, and higher levels of education; it was not significantly related to gender, marital status, intensity of physical activity, duration of sleep, smoking habits, alcohol consumption, or BMI.

### 3.4. Multivariate Logistic Regression Analysis of Isoleucine, Leucine, Valine and Diabetes Mellitus in Elderly Patients

Table 4 showed the results of a crude and multivariate model of three amino acid intakes associated with diabetes. Regardless of coarse model OR multivariate adjustment, dietary isoleucine was still a risk factor for diabetes in the elderly (OR=3.575, 95%CI: 1.321-10.692). Leucine (OR=0.540, 95%CI: 0.357-0.817) was a protective factor for diabetes, but there was no association between valine and diabetes in older adults.

**Table 4. Multivariate Logistic Regression Analysis Of Isoleucine, Leucine, Valine And Diabetes Mellitus In Elderly Patients**

Characteristics	Total		P-value
	OR	95%CI	
Model 1			
Isoleucine	4.384	1.605~11.973	0.004
Leucine	0.484	0.323~0.724	< 0.001
Valine	0.830	0.371~1.861	0.204
Model 2			
Isoleucine	4.228	1.506~11.872	0.006
Leucine	0.526	0.349~0.792	0.002
Valine	0.747	0.330~1.688	0.483
Model 3			
Isoleucine	3.757	1.321~10.692	0.011
Leucine	0.540	0.357~0.817	0.003
Valine	0.785	0.344~1.789	0.537

Note: Model 1 had not been adjusted; Model 2 adjusted gender and age; Model 3 adjusted for sex, age, marital status, education, smoking, alcohol consumption, BMI, and exercise intensity.

## 4. Discussion

As the global population ages, health issues among the elderly are increasingly becoming a focus of concern. This

study aimed to explore the association between branched-chain amino acids (BCAAs) in the diet of community-dwelling elderly people in China and diabetes. Through cross-sectional surveys and statistical analyses, we found a significant correlation between BCAAs in the diet of elderly Chinese community residents, such as isoleucine and leucine, and diabetes. Specifically, isoleucine was identified as a risk factor for diabetes in the elderly (OR=3.575, 95%CI: 1.321~10.692), while leucine acted as a protective factor (OR=0.540, 95%CI: 0.357~0.817). There was no association observed between valine and diabetes. These relationships persisted even after adjusting for covariates.

These findings were consistent with international research results, which indicated that elevated levels of plasma BCAAs were associated with obesity, insulin resistance, and the development of diabetes. [16-18] A Chinese study investigating 429 individuals at various stages of diabetes development found that plasma BCAA markers had predictive value for the future development of diabetes. [19] A meta-analysis in the UK also showed similar results, demonstrating a positive temporal association between plasma BCAA levels and the risk of T2DM. [20] A study in Thailand also found a positive correlation between plasma isoleucine concentrations and the occurrence of type 2 diabetes. [21] Additionally, high levels of BCAAs may be markers of dietary patterns related to diabetes and obesity. [22] A study in Iran on individuals aged 35 to 70 showed a positive correlation between dietary leucine, valine, and isoleucine and type 2 diabetes. [23] Animal experiments further indicated that dietary restriction of isoleucine could increase the health span and lifespan of genetically heterogeneous mice. [24]

BCAAs are abundant in high-protein foods, accounting for about 20% of the amino acids in meats, fish, eggs, and nuts. [25] The metabolism of BCAAs in the body involves multiple pathways, including transamination, deamination, and entry into energy metabolism through the citric acid cycle. Metabolic disorders of BCAAs may lead to amino acid toxicity, oxidative stress, and inflammatory responses, all of which are potential mechanisms for the development of diabetes. [26]

Although this study provided strong evidence of the association between dietary BCAAs and the risk of diabetes, there were some limitations. Firstly, due to the cross-sectional design of the study, a causal relationship cannot be established. Secondly, dietary surveys may be subject to reporting bias, and the intake of BCAAs may be influenced by various food factors, which could affect the accuracy of the results. Additionally, this study did not cover all possible confounding factors, such as genetic background and gut microbiota composition, which may also affect the metabolism of BCAAs and the risk of diabetes.

Based on the findings of this study, future research should consider a prospective cohort study design to further explore the causal relationship between BCAA intake and the risk of diabetes. At the same time, future studies should consider including a broader range of biomarkers, such as metabolic products of BCAAs and the activity of related signaling pathways, to more comprehensively understand the biological connection between BCAAs and diabetes. Furthermore, exploring the

impact of dietary patterns and specific food sources of BCAAs on the risk of diabetes may help develop more targeted nutritional intervention strategies.

In summary, this study revealed a positive correlation between the intake of BCAAs in the diet of elderly Chinese community residents and the risk of diabetes, providing a new perspective on understanding the nutritional metabolism mechanisms of diabetes in the elderly. Future studies should further explore the biological basis of this association and consider developing evidence-based nutritional intervention measures to reduce the risk of diabetes in the elderly.

## 5. Conclusion

This study preliminarily explored the relationship between branched-chain amino acids (BCAAs) in the diet and diabetes mellitus in the elderly. The high intake of isoleucine in the diet was significantly associated with an increased risk of diabetes in the elderly (OR=3.575, 95%CI: 1.321~10.692), while a high intake of leucine was significantly associated with a reduced risk of diabetes (OR=0.540, 95%CI: 0.357~0.817). No association was found between valine and diabetes. This suggests that isoleucine may be a risk factor for diabetes, and leucine may be a protective factor, although the causal relationship with diabetes has not been investigated. Future studies should recruit a larger sample of participants and use long-term follow-up study designs to verify these findings, providing new strategies for the prevention and treatment of chronic diseases.

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## Author Contributions

WCY: conceived the research and designed the study. SYF: analyzed the data, drafted and finalized the manuscript; LZQ,WLL and CTX:contributed to defining the scope of the study and the selection of variables; CHE : conducted study and completed data entry at study sites; WCY: critically reviewed the manuscript. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

## Conflicts of Interest

The authors declare no competing interests.

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