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Association of Dietary Inflammatory Index (DII) and depression in the elderly over 55 years in Northern China: analysis of data from a multicentre, cohort study

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ABSTRACT

Objectives Our study aimed to assess the association between the Dietary Inflammatory Index (DII) and depression in the elderly over 55 years in Northern China.

Methods We analysed the data of 2022 Chinese adults aged 55 and over from a community-based neurological disease cohort study from 2018 to 2019. A validated semiquantitative food frequency questionnaire was used to assess eating habits at the time of inclusion. Multiple logistic regression was used for analysis, and social demographics, lifestyle and health-related factors were adjusted.

Results Among the included population, the prevalence of depression was 23.39%. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and −5.20 to +5.68. The risk of depression was significantly higher in participants in the most pro-inflammatory group (quartile 4) than in the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37 to 1.82; p-trend=0.01). The subgroup analysis of body mass index (BMI) showed that there is a significant association between DII and the risk of depression in overweight and obese people (p < 0.05). The restricted cubic spline results show that the OR value of depression possesses an upward trend with the increase of the DII score.

Conclusions Aged patients with depression present a higher potential for dietary inflammation. Pro-inflammatory diets might increase the risk of depressive symptoms. Further research in different populations is crucial to confirm the association between DII and depression.

Strengths and limitations of this study

► Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors.

► To the best of our knowledge, the current study is the first to explore the association between Dietary Inflammatory Index (DII) and depression in the elderly over 55 years in China.

► Due to all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected.

► Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study.

► Owing to disease-related conditions such as diabetes and high blood pressure that are only based on confounding factors reported by participants, the results may be unreliable.

INTRODUCTION

Due to rapid economic growth and changes in lifestyles, China is undergoing a rapid epidemiological transition from infectious diseases to non-communicable diseases (NCDs). Mental disorders such as depression are an important but often overlooked NCD, and it is becoming an increasingly serious cause of disability and disease burden.[1] These conditions are common in the general population, especially the elderly. For example, 7.73% of elderly people aged 55 and over in China suffered from depression (major depressive disorder (MDD) and dysthymia) in the previous month, and the prevalence is 3.5 times and 1.4 times that of adults aged 18–39 and 40–54 years.[2]

Systemic inflammation is becoming an important factor in the aetiology of mental illnesses such as depression and anxiety.[3] Approximately one-quarter of patients with major depression (MDD) show evidence of systemic inflammation.[4] Moreover, some studies have shown that chronic low-grade inflammation of the whole body can affect monoaminergic and glutamate neurotransmission, which may adversely affect the cognitive function of patients with bipolar disorder or major depression. However, before the first episode of depression, whether various

pro-inflammatory cytokines are abnormally elevated remains unclear.[5] [6] Some studies have shown that the association between diet and mental health disorders may be mediated by the inflammatory properties of diet.[7] The current treatment of depression is not considered to be effective in all cases. So far, there are few nutritional programmes in the guidelines for the treatment of depression. Recently, due to the pro-inflammatory and anti-inflammatory properties of nutrients, people are paying more and more attention to the protective and regulating effects that diet may have in common mental disorders (including depression).[8] However, there are limited data on the role of dietary inflammation potential in this regard.[9] The long-term unhealthy diet leads to a decline in the quality of the diet, which may create a pro-inflammatory environment in the human body, thereby creating conditions for the occurrence and development of various chronic inflammatory diseases. Dietary Inflammatory Index (DII), as a tool that can assess the potential of dietary inflammation, provides the possibility to test this hypothesis.[10]

Meanwhile, inflammation has important physiological effects on mood and behaviour. Kynurenine metabolism is hypothesised to be a pathway connecting inflammation and depression, partly because of the effect of kynurenine metabolites on the neurotransmission of glutamate in the central nervous system.[11] Some studies have shown that inflammation may affect the interconnection of the hypothalamus with areas important for cognition and emotion, and it may cause the hypothalamus–pituitary–adrenal axis to be dysregulated and affect the monoaminergic system.[12]

The DII was developed and verified by researchers at the University of South Carolina in Columbia to assess the inflammatory potential of an individual's diet. The initial DII score was based on the results of articles published from 1950 to 2007 that assessed the impact of specific foods on specific inflammatory markers (specific inflammatory markers include interleukin(IL)-1β, IL-4, IL-6, IL-10, tumour necrosis factor α (TNF-α) and C reactive protein (CRP)). These foods significantly increase IL-1β, IL-6, TNF-α or CRP, or decrease IL-4 or IL-10 to '+1', which is pro-inflammatory; and significantly reduce IL-1β, IL-6, TNF -α or CRP, or increase IL-4 or IL-10 to '−1', which is an anti-inflammatory effect. In 2014, South Carolina researchers improved the DII score from 2007 to 2010, and the improved scoring system applied 45 food parameters.[13]

The relationship between diet, inflammation and mental health is of increasing interest, and the link between diet and mental health disorders may be mediated by the inflammatory properties of diet.[7] As a tool to assess the potential of dietary inflammation, the relationship between DII and mental disorders is worthy of discussion and research. Moreover, a study has shown that people with the lowest levels of DII have a lower risk of being at the highest levels of mental health disorders.[7]

Although the number of patients with depression has increased in recent years, compared with other developed countries, there are relatively few studies on depression in China.[14] Therefore, it is urgent to explore the relationship between DII and depression risk in the Chinese elderly. The DII is a tool used to quantify the dietary inflammation potential of an individual's diet. Its goal is to assess the impact of diet-related inflammation on health outcomes.[15] Thus, the purpose of this work was to examine the association between the inflammatory potential of habitual diets and depression. Moreover, the use of DII as an indicator to directly and reasonably connect the three of nutrition, inflammation and depression, may have clinical and public health significance for the development of new nutritional psychiatric methods to promote good mental health.

METHODS

Study population

Participants came from the Community Cohort Study of Nervous System Diseases (CCSNSD) project under the National Key Research and Development Program and the Precision Medicine Project Nervous System Disease Cohort Research project. The project is undertaken by the Institute of Nutrition and Health of the Chinese Center for Disease Control and Prevention, in cooperation with the Center for Disease Control and Prevention. The project uses a multistage random cluster sampling method to draw samples.

In allusion to subjects recruited in the CCSNSD cohort, the samples eligible for inclusion were (1) 55 years old and older, (2) resident population living in the sampled community, (3) absence of clinically diagnosed depression, (4) be able to perform a normal depression assessment, (5) completed data of sociodemographic characteristics, disease history and food frequency questionnaire (FFQ). We excluded subjects because of (1) no depression assessment results, (2) lack of baseline status such as education and physical activities, (3) nutrient deficiency, (4) abnormal energy intake and (5) people with other psychological disorders. Finally, a total of 2022 participants were involved in the analysis.

Patient and public involvement

Written informed consent was obtained from all participants.

Depression

We defined depression according to the Geriatric Depression Scale (GDS); this scale is one of the most widely used scales to assess the depression of the elderly.[16] It consists of 30 self-assessment items with yes/no response options. A score of 0–10 indicates no depression, a score of 11–20 indicates mild depression, and a score of 21–30 indicates severe depression.[17]

Assessment of food consumption

Dietary consumption is assessed by a validated semiquantitative FFQ, covering 81 foods. Participants were asked

about the frequency of habitual consumption and the number of each item in the past 12 months, and choose from five types of frequencies (daily, weekly, monthly, yearly or never) and consumption in the past 12 months. For consumers, their consumption of each food group or item is calculated based on their reported average consumption frequency and quantity.

Assessment of DII score

The DII aims to provide a quantitative method for assessing the effect of diet on health outcomes.[18] It is the characteristic of DII to objectify the inflammatory characteristics of specific dietary intake.[19]

The calculation of the DII links the personal dietary data obtained in each clinical study with the global average intake. The specific formula is: Z score = (daily intake of this kind of dietary ingredient or nutrient–this kind of dietary ingredient or the global average per capita daily intake of nutrients)/the SD of the global average per capita daily intake of this dietary ingredient or nutrient. Then, convert the Z score to a percentile system (to reduce the influence of outlier effects), double the obtained percentile value and subtract '1' to achieve a symmetrical distribution centred on '0'. Finally, multiply by the total inflammatory score of each dietary component, and combine the results to obtain the personal DII score. DII scores range from negative tail to positive tail; more negative values indicate anti-inflammatory properties and corrected scores indicate pro-inflammatory properties.[7] Energy-adjusted DII food intake per 1000 calories is used to explain the effect of total intake on energy intake. For this, the energy standardised version requires a world database.[20] Twenty-two of the 45 possible food parameters were used for DII calculation based on the FFQ in this study (carbohydrates, protein, fat, β-carotene, fibre, cholesterol, saturated fat, monounsaturated fat, polyunsaturated fat, niacin, thiamine, riboflavin, vitamin B_{12}, vitamin B_6, iron, magnesium, zinc, selenium, vitamin A, vitamin C, vitamin E and folic acid).

The appendix of the DII

$Zscore = [(daily mean intake - global daily mean intake)/SD]$

$Zscore^1 = Zscore \rightarrow (converted to a percentile score) \times 2 - 1$

$DII = \sum Zscore^1 \times$ the inflammatory effect score of each dietary component

Covariates

We adjusted the covariates including self-reported age (yearly), gender (female or male), an education level (illiterate, elementary school, junior high school and above), employment status (yes or no); health-related variables including tobacco smoking (yes or no), alcohol drinking (yes or no), physical activity (yes or no), daily energy intake(kcal), diabetes (yes or no), and hypertension (yes or no). We use a cut-off value of 28 kg/m^2 of China's body mass index (BMI) to determine obesity.[21]

Statistical analysis

Data were expressed as mean (SD/SEM) and n (%) for continuous variables and categorical variables, respectively. The differences between groups were analysed by analysis of variance of continuous variables and χ^2 test of categorical variables. Logistic regression analysis is used to simulate the association between depressed people and people in different DII quartiles, and OR (95% CI) was calculated to evaluate the relationship between depression and the DII score. We used a subgroup analysis of BMI to optimise the robustness of the statistical test (BMI <18.5, 18.5–24.0, 24–28, ≥30 kg/m^2). Restricted cubic splines were used to evaluate the correlation between the DII and the risk of depression. All statistical analyses were performed using the software package R (http://www.R-project.org, The R Foundation). A two-tailed p value of <0.05 was considered statistically significant.

RESULTS

From the Community Cohort Study on Specialized Nervous System Diseases, the study included 2022 elderly participants (median (IQR) age, 64 (60-70) years; 775 (38.3%) males) from 2017 to 2018. Mean (SD) and range of the DII in the included population were 1.70 (1.42) and –5.20 to +5.68. Clinical and demographic characteristics according to quartiles of DII are presented in online supplemental table 1. A higher incidence of depression was observed among individuals in the highest quartile of the DII, and thus the most pro-inflammatory diet. Individuals in the highest quartile of DII were more likely to be patients with obesity, hypertension and to have less daily energy intake. No differences in sex, employment status, physical activities, diabetes, tobacco smoking or alcohol drinking were observed between groups. We also compared baseline characteristics of patients with and without depression, and found differences in gender, employment status and physical activity between the two groups (p < 0.05) (online supplemental table 2). At the same time, no significant difference was observed between the nutrients between the two groups (online supplemental table 3).

Table 1 shows the OR and 95% CI of depression according to the quartile of DII. When DII is expressed as a quartile, the results obtained by adjusting for confounding factors and modelling DII as a categorical variable for depression indicate that there is a direct association. The risk of depression was significantly higher in participants in the most pro-inflammatory group (quartile 4) than in the participants in the most anti-inflammatory group (quartile 1) (OR 1.53; 1.37 to 1.82; p-trend=0.01).

Stratified logistic regression analysis (table 2) revealed BMI differences in the associations between dietary inflammatory potential and depression outcomes (BMI<18.50 kg/m^2; 18.50≤BMI<24.00; BMI≥28.00). Increased risk of depression was observed among the overweight and obese study participants, respectively (OR 1.25, 95% CI 1.08 to 1.46; OR 1.39, 95% CI 1.19 to 1.52). Comparing the highest to the lowest quartile of DII, the association

Table 1 Logistic regression analysis of the association between Dietary Inflammatory Index (DII) and depression

	Quartile 1 (n=504)	Quartile 2 (n=506)	Quartile 3 (n=504)	Quartile 4 (n=508)
Model 1	1 (reference)	1.29 (1.09–1.42)	1.36 (1.13–1.52)	1.43 (1.29–1.68)
Model 2	1 (reference)	1.33 (1.12–1.46)	1.40 (1.27–1.65)	1.51 (1.31–1.75)
Model 3	1 (reference)	1.31 (1.20–1.43)	1.39 (1.25–1.63)	1.53 (1.37–1.82)

Model 1 is not adjusted.
Model 2 adjusts age, sex, BMI, employment, education, daily energy intake, daily energy intake, tobacco smoking, alcohol drinking and physical activities.
Model 3 adjusts age, sex, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.
BMI, body mass index.

with depression remained in the fully adjusted model ($p < 0.05$, comparing highest to lowest tertile of DII). No associations were observed among the underweight and normal-weight participants. The Restricted Cubic Spline (RCS) results show that the OR value of depression possesses an upward trend with the increase of the DII score ($p < 0.05$; figure 1). At the same time, a subgroup analysis of people of different genders showed that the pro-inflammatory diet is a risk factor for depression in elderly women ($p < 0.05$; table 3).

DISCUSSION

As far as we know, this is the first study in China to investigate the association between depression and DII as a representative indicator of the potential for dietary inflammation. We found that patients with depression had higher DII scores compared with the control group without depression. The association between DII and depression observed in this study suggests that the potential of an inflammatory diet plays an important role in depression.

The significant association between DII and depression observed in the current study broadly supports a related study that studied 254 patients with depression in the UK and found that compared with the disease-free control group, these patients' DII scores were higher.[22] Other reports have found that compared with other types of severe mental illness, people with depression have higher

Table 2 Body mass index stratified analysis of the association between Dietary Inflammatory Index (DII) and depression

	Model 1	Model 2	Model 3
BMI <24.00 (normal weight)			
Quartile 1 (n=180)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2 (n=232)	1.08 (0.92–1.18)	1.06 (0.82–1.16)	1.05 (0.86–1.18)
Quartile 3 (n=221)	1.12 (0.86–1.25)	1.15 (0.92–1.28)	1.18 (0.92–1.26)
Quartile 4 (n=189)	1.16 (0.95–1.28)	1.21 (0.96–1.46)	1.32 (0.98–1.52)
P-trend	0.28	0.16	0.08
24.00≤BMI<28.00 (overweight)			
Quartile 1 (n=215)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2 (n=194)	1.09 (0.89–1.25)	1.08 (1.01–1.26)	1.10 (1.03–1.29)
Quartile 3 (n=184)	1.13 (1.02–1.32)	1.15 (1.05–1.29)	1.21 (1.09–1.37)
Quartile 4 (n=187)	1.25 (1.08–1.46)	1.31 (1.11–1.52)	1.35 (1.13–1.56)
P-trend	0.03	0.01	0.006
BMI≥28.00 (obese)			
Quartile 1(n=109)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2 (n=80)	1.08 (1.01–1.19)	1.15 (1.05–1.29)	1.18 (1.09–1.35)
Quartile 3 (n=99)	1.21 (1.10–1.39)	1.28 (1.13–1.46)	1.32 (1.19–1.58)
Quartile 4 (n=132)	1.39 (1.19–1.52)	1.42 (1.21–1.62)	1.56 (1.23–1.78)
P-trend	0.008	0.005	0.003

Model 1 is not adjusted.
Model 2 adjusts age, sex, employment, education, daily energy intake, tobacco smoking, alcohol drinking and physical activities.
Model 3 adjusts age, sex, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.
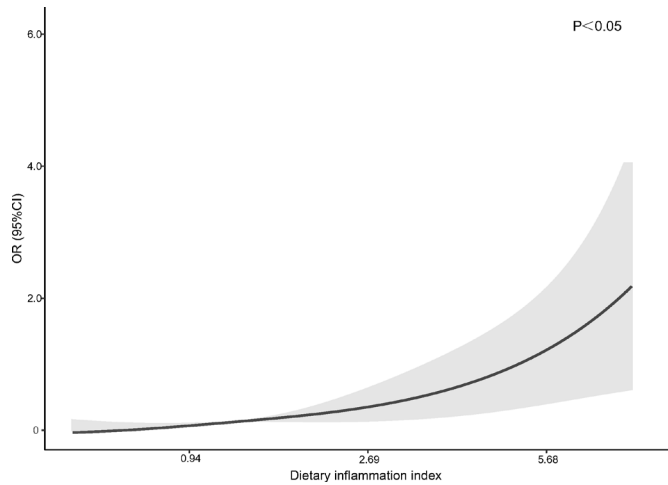BMI, body mass index.

P<0.05

Figure 1 Restricted cubic splines for the non-linear relationship between the risk of depression and increased Dietary Inflammatory Index.

levels of dietary inflammation and are more likely to show worse indicators of physical health.[23]

Depression (or clinical depression) is a widespread and severe mood disorder worldwide.[24] Among the elderly, depression is the most common mental disorder, and it is becoming more common. Depression also reduces the ability of the elderly to recover.[25] Therefore, the National Institute of Mental Health in the USA regards depression in the elderly as a major public health problem, leading to significant and continuous growth in healthcare expenditures. In addition, depression is often associated with an increased risk of other diseases (such as heart disease) and mortality in the elderly.[26 27] Therefore, personalised early depression detection is essential for the physical and mental health of the elderly. Effective and individualised prediction of the onset of depression can inform

intervention strategies in time to prevent depression in the elderly and further reduce the cost of medical care. A study in US women also applied reduced rank regression (using CRP, IL-6 and TNF-A as response variables) and found that higher scores in inflammatory dietary patterns, including sugary beverages, refined grains, red meat, dietary soft drinks, margarine, and other vegetables and fish, were associated with higher depressive symptoms. In addition, three studies using prior DII observed a statistically significant positive association between higher DII scores and higher depressive symptoms.[28 29]

As we all know, inflammation is related to depression. In the early 1990s, the macrophage theory was first hypothesised as depression, especially when these cells are activated by any damage (M1 cells).[30] There is increasing evidence that the accumulation of M1 cells (including microglia and central nervous system macrophages) plays a critical role in the pathogenesis of depression, as peripheral M1 cells may be the main source of cytokine increase in depression. Due to changes in the peripheral immune system of depression, cellular immunity is impaired, resulting in increased levels of pro-inflammatory cytokines.[31 32] For example, cytokines may affect neurotransmitter metabolism, neuroendocrine function and regional brain activity. All of these factors may be related to the onset of depression. However, it should be noted that in studies that adjusted the analysis of serum cytokine levels, DII was still significantly associated with the onset of depression. These findings may indicate that unhealthy (pro-inflammatory) diets independently lead to the onset of depression, further leading to important clinical consequences. Dietary intervention seems to be an important goal in preventing depression. Some observational studies have reported that a healthy diet (such as the Mediterranean diet) is associated with

Table 3 Gender stratified analysis of the association between Dietary Inflammatory Index (DII) and depression

	Model 1	Model 2	Model 3
Male			
Quartile 1 (n=201)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2 (n=191)	1.09 (0.87–1.21)	0.98 (0.62–1.12)	1.06 (0.90–1.19)
Quartile 3 (n=190)	1.06 (0.68–1.15)	1.08 (0.89–1.18)	1.14 (0.98–1.28)
Quartile 4 (n=193)	1.12 (0.91–1.27)	1.16 (0.98–1.32)	1.26 (1.02–1.36)
P-trend	0.41	0.28	0.06
Female			
Quartile 1 (n=303)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
Quartile 2 (n=315)	0.96 (0.81–1.08)	1.07 (1.01–1.18)	1.12 (1.04–1.28)
Quartile 3 (n=314)	1.08 (0.96–1.25)	1.17 (1.06–1.31)	1.21 (1.08–1.35)
Quartile 4 (n=315)	1.17 (1.02–1.35)	1.26 (1.08–1.37)	1.36 (1.15–1.42)
P-trend	0.042	0.028	0.016

Model 1 is not adjusted.
Model 2 adjusts age, BMI, employment, education, daily energy intake, tobacco smoking, alcohol drinking and physical activities.
Model 3 adjusts age, BMI, employment, education, tobacco smoking, alcohol drinking, physical activities, diabetes and hypertension.
BMI, body mass index.

a lower incidence of depression in adults. Our research further confirms these findings, suggesting that a healthy diet may be necessary to prevent depression. A recent randomised controlled trial of adults with depressive symptoms showed that using a Mediterranean diet significantly reduced depressive symptoms. In addition, it can be assumed that there is a synergistic anti-inflammatory effect between antidepressants and the Mediterranean diet or the longevity diet, so as to propose prevention and intervention before or when mild symptoms appear.[33–36]

The lifetime prevalence of major depressive disorder (MDD) and depressive symptoms in women is higher than in men. Studies have shown that the estimated number of women with mood disorders is about twice that of men. Stressful life events, health and lifestyle factors, and a history of premenstrual dysphoria are related to the prevalence of MDD and depressive symptoms during menopausal transition.[37 38] There is evidence to indicate that changes in reproductive hormone levels are predisposing factors for depression in women who are susceptible to depression. The immune response changes with ageing. For women, menopause is an important life event that changes the immune response, because the ovarian hormone oestrogen has anti-inflammatory effects and plays a protective role in innate immunity. It is worth noting that the epidemic of depression increases the risk of vascular diseases such as coronary heart disease and atherosclerosis by activating inflammation and causing endothelial cell dysfunction. Although men have a higher risk of cardiovascular disease than women during the entire life cycle, as the frequency of depressive symptoms increases, women's cardiovascular risk in later life increases significantly. Studies have shown that there are significant gender differences in the gene expression patterns of white blood cells in patients with late-life depression (LLD). Differentially Expressed Genes (DEGs) in white blood cells of patients with LLD are related to innate immune function, especially in women. Since inflammation is known to be related to the pathophysiology of MDD and depressive symptoms, changes in the activity of the innate immune system may contribute to the pathophysiology of female LLD. In addition, MDD itself or diseases that are comorbid with MDD may lead to increased inflammatory activity, especially in elderly women. In contrast, inflammation may be an uncommon feature in the pathophysiology of male LLD.[38–40]

The subgroup analysis of BMI showed that there is a significant association between DII and the risk of depression in overweight and obese people. Eating behaviour related to mood may be the underlying mechanism of the relationship between depression and obesity. Several mechanisms can explain the link between depression and obesity in this pathway. In particular, emotional eating, food reward processes, increased brain monoamine activity and the inflammatory potential of the diet may also be related to the depression–obesity link. Future studies must be conducted to examine whether the intake of pro-inflammatory foods can enhance the emotional

state of patients with atypical depression under psychosocial stress.[41 42]

Among the strengths of our study are a large number of participants over 55 years with evaluable data; information about diet and lifestyle factors; and various confounding factors. To the best of our knowledge, the current study is the first to explore the association between DII and depression in the elderly over 55 years in China. None of the 30 items in the GDS was somatic, thus avoiding the confusion of somatic symptoms with physical disturbances that were common in the elderly. The limitation is also of note. First, because all of the participants recruited into the cohort are from the same province, the true state of the nation's elderly may not be accurately reflected. Another potential limitation is that among the 45 food parameters, only 22 food parameters can be used in the DII calculations in this study, and there may be deviations in the estimation of the possibility of dietary inflammation. Furthermore, the dietary consumption level is estimated based on the FFQ covering the past 12 months, which may have a certain recall bias. Finally, because disease-related conditions such as diabetes and high blood pressure are only based on confounding factors reported by participants, the results may be unreliable.

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