Effects of nuts and unsaturated fatty acids on Nonalcoholic Fatty Liver Disease

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Research Article

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Abstract

Objective

To analyze the influence of nuts and unsaturated fatty acids on Nonalcoholic Fatty Liver Disease (NAFLD) and put forward reasonable suggestions for prevention.

Methods

A total of 696 patients (483 males and 213 females) admitted to Tang Du Hospital from September 2019 to May 2021 were included in the study. The effects of several factors on NAFLD were analyzed by Logistic regression, and the OR value was calculated. Smooth curves were plotted and stratified by sex, hyperlipidemia, diabetes, and hypertension.

Results

nut intake (OR= 0.97678, 95% CI [0.95581, 0.99822], P=0.033894. RR= 0.9812) and polyunsaturated fatty acids (OR= 1.20633, 95% CI [1.12796, 1.29014], P<0.000001. RR= 1.1601) had an effect on NAFLD. The risk of NAFLD was the lowest when nut intake was 2.82 g/day, while the risk of NAFLD was highest when the intake of polyunsaturated fatty acids was 30.02 g/day.

Conclusions

we recommend 2.82g/day for nuts. Men are more suitable for eating nuts than women. Patients with hyperlipidemia should consume more nuts appropriately, and patients with diabetes should consume 3.74g/day. Polyunsaturated fatty acids should also be reduced to less than 30.02 g/day.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common liver disease worldwide and is now the second leading indication for liver transplantation (LT) in the United States[1, 2]. Currently, the global incidence of NAFLD is approximately 25%[3]. In addition, the proportion of patients with hepatocellular carcinoma (HCC) as a potential cause of nonalcoholic steatohepatitis (NASH) increased by 7.7 times (from 2.1–16.2%)[4]. And the proportion of NASH patients has continued to increase in recent years[5]. Currently reported rates of NASH range from 1.5–6.45%[6, 7], and 7–30% of patients with NAFLD have NASH[7, 8], which is likely to be underestimated given that diagnosis requires histological biopsy. In addition, in the population, men take a higher risk of NAFLD, which may be related to the anti-fibrosis effects of estrogen[9]. Although the incidence of NAFLD is increasing year by year, the progression of NAFLD will also lead to the increase of cardiovascular and liver related risks, there is no effective
treatment drugs, the diet control and lifestyle change is still an important means of prevention and treatment.

Nuts are nutrient-rich foods that contain bioactive compounds beneficial to health: plant protein, unsaturated fatty acids, fiber, minerals, vitamins, tocopherols, phytosterols and polyphenols[10]. Although some studies have also carried out studies on the effects of nuts on cardiovascular and liver diseases, the results may be different due to the differences in the composition of nuts in different studies[11]. However, in the overall study, nut consumption was associated with protection against type 2 diabetes mellitus(T2DM)[12, 13], metabolic syndrome (MetS)[13, 14], obesity[15, 16] and arterial hypertension[17], and was also associated with reduced inflammation[18, 19] and insulin resistance(IR)[20]. Since inflammation, oxidative stress and IR are believed key drivers of NAFLD[21, 22], it is reasonable to assume that nuts have an impact on the progression of NAFLD. A recent study reported a significant reduction in NAFLD in patients who consumed nuts more than 4 times per week, but the study was incomplete. Nut intake, monounsaturated fatty acid (MUFA) intake and polyunsaturated fatty acid (PUFA) intake may be important factors affecting NAFLD, which is also an important purpose of this study.

**Methods**

**Patients and design**

A total of 696 patients (483 males and 213 females) admitted to Tang Du Hospital from September 2019 to May 2021 were included in the study, and a total of 162 (23.2759%) patients were diagnosed with NAFLD. After simple training, all patients were able to complete the questionnaire independently, and the dietary and lifestyle information was obtained through the questionnaire. This study was approved by the Ethics Committee of Tang Du Hospital, and all patients signed informed consent.

**Diagnose**

NAFLD in this study was diagnosed by an experienced ultrasound physician through B-mode ultrasound.

**Statistical analyses**

Statistical analyses were performed using R 4.1.1. The effects of nut intake, age, gender, smoking, drinking tea, monounsaturated fatty acids and polyunsaturated fatty acids on NAFLD were analyzed by Logistic regression, and the OR value was calculated. Smooth curves were plotted and stratified by sex, hyperlipidemia, diabetes, and hypertension.

**Result**

**Patient characteristics**

This study included 696 subjects, including 483 males (69.3966%), 213 females (30.6034%). 162 subjects (23.2759%) were diagnosed with NAFLD. The characteristics of the study population can be
The relationship between NAFLD and various factors

The effects of nut intake, intake frequency and unsaturated fatty acids intake on NAFLD can be seen in Table 2. Only nut intake (OR= 0.97678, 95% IC [0.95581, 0.99822], P=0.033894. RR= 0.9812) and polyunsaturated fatty acids (OR= 1.20633, 95% IC [1.12796, 1.29014], P<0.000001. RR= 1.1601) had an effect on NAFLD. Daily energy intake, frequency of nut intake, and monounsaturated fatty acids were not statistically significant.

Effects of nut intake and polyunsaturated fatty acid intake on NAFLD

The smooth curve of the influence of nut intake on NAFLD was shown in Figure 1a, which decreased from the beginning to 2.82 and then began to rise, indicating that the risk of NAFLD decreased first and then increased with nut intake. The risk of NAFLD was the lowest when nut intake was 2.82 g/day. The smoothing curve of the influence of polyunsaturated fatty acids on NAFLD is shown in Figure 1b. The risk of NAFLD increased with the increase of the intake of polyunsaturated fatty acids and reached the peak at 30.02g/day, indicating that the risk of NAFLD was highest when the intake of polyunsaturated fatty acids was 30.02g/day.

Stratified analysis of nut intake

The effect of nut intake on NAFLD in different genders was shown in Figure 2a. In women, the risk of NAFLD increased with the increase of nut intake, while in men, the risk decreased with the increase of nut intake, with a fluctuation of 2.8 g/day. This could mean that men were better suited to nuts than women.

The influence of nut intake on NAFLD in patients with hyperlipidemia was shown in Figure 2b. In patients without hyperlipidemia, the risk of NAFLD decreased first and then increased with the increase of nut intake, and the inflection point of the curve was 40.25g/day. In patients with hyperlipidemia, the risk of NAFLD decreased with the intake of nuts. This means nuts are better for people with hyperlipidemia.

The influence of nut intake on NAFLD in hypertension was shown in Figure 2c. Nut intake in hypertensive patients decreased first and then increased; among hypertensive patients, nut intake of 19.75g/day was associated with the highest risk of NAFLD. Regardless of whether the population has hypertension, 2.82g/day is still recommended for nuts.

The effect of nut intake on NAFLD in diabetes was shown in Figure 2d. The risk of NAFLD was lowest in patients with diabetes when nut intake was 3.74g/day, and lowest in patients without diabetes when nut intake was 2.82g/day.

Stratified analysis of polyunsaturated fatty acid intake.

The influence of polyunsaturated fatty acid intake on NAFLD can be seen in Figure 3. The risk of NAFLD increased with the increase of intake in women, but decreased first and then increased in men, reaching
the highest at 30.02g/day. For people without hypertension, hyperlipidemia and diabetes, the curve reached the highest at about 30.02g/day, while for people with hypertension, hyperlipidemia and diabetes, the risk of NALFD increased with the increase of the intake of polyunsaturated fatty acids.

**Conclusion**

NAFLD is the most common liver disease, occurring in about 90% of obese patients and 50% of diabetics[23, 24]. According to current reports, NAFLD is often associated with metabolic syndrome, including diabetes, hyperlipidemia, obesity, hypertension, etc[25]. Women take a lower risk of NAFLD than men, due to hormone levels in women, possibly due to the anti-liver fibrosis effect of estrogen[26]. A decrease in estrogen can cause fat accumulation in the liver, which increases the risk of NAFLD[27]. Studies have shown that after menopause, women take a significantly increased risk of NAFLD and more severe liver fibrosis[28, 29]. This is consistent with our findings that men are more suitable to consume nuts than women. In women after menopause, nut consumption may have a different effect on NAFLD than before menopause. However, fewer post-menopausal women were included in this study, which still needs further research.

Nut consumption was associated with a lower risk of NAFLD. It determined by the specific nutritional composition of nuts. Studies have shown that a Mediterranean diet including nuts may significantly improve insulin resistance, which is present in almost all NAFLD patients[30]. α-linolenic acid in nuts can up-regulate insulin receptors[31], bioactive fatty acids regulate the activity of liver cells[32], Dietary fiber, vitamin E and phenolic compounds have anti-inflammatory and antioxidant effects[33], all of these nutrients can reduce the risk of NAFLD. In addition, the imbalance of intestinal flora is also an important cause of NAFLD, and nuts can regulate intestinal flora, thereby reducing the risk of NAFLD[34–36]. This study also showed that nut intake can reduce the risk of NAFLD, and for patients with hyperlipidemia, nut intake is recommended, and for patients with diabetes, it should be 3.74g/day. Hypertension seems to have little effect on nuts and NAFLD, and there is no need to adjust nut intake for these patients.

Although some studies have suggested that C20-22 ω3 Polyunsaturated fatty acids reduce the risk of NAFLD in part by controlling the activity and/or abundance of transcription factors that regulate the expression of genes encoding proteins involved in liver fat metabolism[37–39]. Besides that, polyunsaturated fatty acids and monounsaturated fatty acids effectively limit liver steatosis through a series of biochemical events, such as reducing NAFLD degeneration markers, increasing lipid metabolism gene expression, and reducing adipogenic activity[40]. However, in the study, we found that monounsaturated fatty acids had no effect on NAFLD, while the intake of polyunsaturated fatty acids may increase the risk of NAFLD. There may be the following reasons: (1) the effect of unsaturated fatty acids on NAFLD needs to be further studied, and there is still not enough evidence to show that it can reduce the risk of NAFLD. (2) Perhaps due to the intake dose of unsaturated fatty acids, we suggest that the intake of polyunsaturated fatty acids should be less than 30.02g/day, while the intake of monounsaturated fatty acids needs further study.
In conclusion, after analysis, we recommend 2.82g/day for nuts. Men are more suitable for eating nuts than women. Patients with hyperlipidemia should consume more nuts appropriately, and patients with diabetes should consume 3.74g/day. Polyunsaturated fatty acids should also be reduced to less than 30.02 g/day.

**Declarations**

**Statements**

**Acknowledgement**

None.

**Author Contributions**

Study concept and design: Yan XU, Yan ZHANG

Data extraction: Yan XU;

Data analysis and interpretation: Yan XU.

Drafting of the manuscript: Yan XU;

critical revision of the manuscript for important intellectual content: Yan ZHANG.

Statistical analysis: Yan XU.

**Statement of Ethics**

1. Institutional Ethics Committee, Tang Du Hospital, Fourth military medical university, Xi an, China.

2. After consulting the Ethics Committee of Tang Du Hospital, this article does not need ethical approval.

**Disclosure Statement**

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None.

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Tables 1-2

Tables 1-2 are not available with this version.

Figures
Figure 1

Smooth curves of the effects of nut intake and polyunsaturated fatty acids on NAFLD. X2: NAFLD, X4: nut intake, X20: polyunsaturated fatty acid intake. a: the smooth curve of the influence of nut intake on NAFLD. b: the smooth curve of the influence of polyunsaturated fatty acid intake on NAFLD.

Figure 2


Figure 3