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Association between time-restricted eating and non-alcoholic fatty liver disease in a nationwide cross-sectional study

Xueke Zeng[1,2,3,4]†, Shaoyu Xie[5]†, Fei Jiang[1]†, Xiude Li[1]†, Meiling Li[1], Tengfei Zhang[1], Yaozong Zhang[1], Songxian Rao[1], Yufeng Mo[1], Honghua Zhang[1], Shu Ye[1], Mengfei Liu[1], Haowei Li[1], Yu Zhu[1], Yong Huang[1], Danni Wang[6]‡ and Wanshui Yang[1,2,3,4]*‡

[1]*Department of Nutrition, School of Public Health, Anhui Medical University, Hefei 230032, Anhui, People's Republic of China*
[2]*Key Laboratory of Population Health Across Life Cycle (Anhui Medical University), Ministry of Education of the People's Republic of China, Hefei 230032, Anhui, People's Republic of China*
[3]*NHC Key Laboratory of Study on Abnormal Gametes and Reproductive Tract, Hefei 230032, Anhui, People's Republic of China*
[4]*Anhui Provincial Key Laboratory of Population Health and Aristogenics/Key Laboratory of Environmental Toxicology of Anhui Higher Education Institutes, Anhui Medical University, Hefei, Anhui, People's Republic of China*
[5]*Department of Chronic Non-communicable Diseases Prevention and Control, Lu'an Municipal Center for Disease Control and Prevention, Lu'an, Anhui, People's Republic of China*
[6]*Teaching Center for Preventive Medicine, School of Public Health, Anhui Medical University, Hefei 230032, Anhui, People's Republic of China*

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Abstract

The association between time-restricted eating (TRE) and the risk of non-alcoholic fatty liver disease (NAFLD) is less studied. Moreover, whether the association is independent of physical exercise or diet quality or quantity is uncertain. In this nationwide cross-sectional study of 3813 participants, the timing of food intakes was recorded by 24-h recalls; NAFLD was defined through vibration-controlled transient elastography in the absence of other causes of chronic liver disease. OR and 95 % CI were estimated using logistic regression. Participants with daily eating window of ≤ 8 h had lower odds of NAFLD (OR = 0·70, 95 % CI: 0·52, 0·93), compared with those with ≥ 10 h window. Early (05.00–15.00) and late TRE (11.00–21.00) showed inverse associations with NAFLD prevalence without statistical heterogeneity ($P_{heterogeneity}$ = 0·649) with OR of 0·73 (95 % CI: 0·36, 1·47) and 0·61 (95 % CI: 0·44, 0·84), respectively. Such inverse association seemed stronger in participants with lower energy intake (OR = 0·58, 95 % CI: 0·38, 0·89, $P_{interaction}$ = 0·020). There are no statistical differences in the TRE-NAFLD associations according to physical activity ($P_{interaction}$ = 0·390) or diet quality ($P_{interaction}$ = 0·110). TRE might be associated with lower likelihood of NAFLD. Such inverse association is independent of physical activity and diet quality and appears stronger in individuals consuming lower energy. Given the potential misclassification of TRE based on one- or two-day recall in the analysis, epidemiological studies with validated methods for measuring the habitual timing of dietary intake are warranted.

Key words: Time-restricted eating: Vibration-controlled transient elastography: Non-alcoholic fatty liver diseases: Eating pattern: Cross-sectional study

Non-alcoholic fatty liver disease (NAFLD) has become the leading cause of liver-related morbidity and mortality and was present in over 30 % of the adult population worldwide[1]. Nonetheless, there have been no approved pharmacological agents for the treatment of such diseases. Lifestyle modification including diet and physical exercise to achieve weight loss is the first-line intervention in patients with NAFLD[2–4]. Although several dietary patterns including Mediterranean diet[2,5] are typically recommended, dietary adherence remains an issue[6].

Currently, intermittent fasting (IF) has gained much attention for weight loss and metabolic benefit[7]. Time-restricted eating (TRE) is an IF regiment that limits the food intake to certain hours

Abbreviations: HEI-2015, Healthy Eating Index-2015; IF, intermittent fasting; NAFLD, non-alcoholic fatty liver disease; NHANES, US National Health and Nutrition Examination Survey; TRE, time-restricted eating; VCTE, vibration-controlled transient elastography.

* **Corresponding author:** Wanshui Yang, email wanshuiyang@gmail.com

† These authors contributed equally as co-first authors
‡ These authors contributed equally as co-corresponding authors

(e.g. 6–10 h) in the day, allowing the daily fasting period to last > 14 h. Such eating pattern does not necessarily alter diet quality or quantity, which may improve adherence[8]. TRE aims to maintain a stable daily cycle of eating and fasting to sustain robust circadian rhythms in mRNA and proteins, which regulate metabolic progress including gluconeogenesis, glycolysis, protein synthesis, lipid synthesis and oxidation and mitochondrial function[8]. In mouse models, TRE has been shown to reduce body weight, increase total energy expenditure and improve glycaemic and lipid profiles and hepatic fat content[6,9,10]. In line with these evidence, an increasing number of TRE interventional studies in normal, overweight, obese and metabolically unhealthy populations showed improvements in body weight and multiple markers of cardiometabolic health[6].

However, limited intervention studies have investigated the effect of IF among patients with NAFLD[10–12]. Only one study focused on TRE (self-selected 8 h window) and showed a significant reduction in weight, fat mass and serum TAG, but not in other lipid profiles, blood pressure, glucose or liver stiffness after 12 weeks of intervention, compared with control group (consumed 80 % of their energy requirement without altering diet quality)[12]. Beyond TRE, two studies have examined the effectiveness of two other forms of IF including modified alternate-day fasting (alternated between days of *ad libitum* eating and days of fasting with total energetic intake of 30 % of requirement)[11] and intermittent energy restriction (the 5:2 diet, fasting for two nonconsecutively days per week with total energetic intake of 500 kcal/day for women and 600 kcal/d for men)[10] among NAFLD patients. In addition, whether different TRE duration (8–10 h *v.* < 8 h eating window (i.e., time interval between first and last time of consuming food or beverage containing energy content in a day)) and timing (early TRE (eating window between 05.00 and 15.00) *v.* late TRE (eating window between 11.00 and 21.00)) have different health effects is unanswered. This issue is important, given the acceptability and long-term feasibility of following TRE. Early TRE and/or shorter eating window could be less feasible and sustainable and may reduce the long-term compliance[13], whereas few studies[14,15] have compared the adherence and effect of early and late TRE. Moreover, it remains unclear that the potential beneficial association between TRE and the risk of NAFLD is independent of physical activity and diet quality and quantity.

To address these issues, we conducted a pilot study to investigate the cross-sectional association between TRE and the odds of NAFLD using data from the US National Health and Nutrition Examination Survey (NHANES). Although TRE was considered as an interventional strategy commonly used in the clinical trials, approximately 10 % of free-living US adults habitually maintain a daily fasting for ≥ 12 h[16], which enables us to evaluate the TRE-NAFLD association in the observational study.

Methods

Study population

The NHANES is a continuous, nationwide cross-sectional survey to assess the health and nutritional status of a sample representative of the civilian noninstitutionalised US population. Details of the NHANES study design and data collection methods have been described elsewhere[17]. All participants provided the written informed consent. The Research Ethics Review Board of the National Centers for Health Statistics approved the study protocols (Protocol #2011–17; Protocol #2018–01).

Participants from the 2017–2018 cycle of NHANES (*n* 9254) were selected, in which vibration-controlled transient elastography (VCTE) examination was performed for the first time in the survey. Individuals ate before 05.00 or after 21.00 in one day (*n* 1669), only had one meal a day (*n* 172), were younger than 18 years (*n* 2568), had implausible energy intake (< 600 or > 3500 kcal/d for women and < 800 or > 4200 kcal/d for men, *n* 195), did not receive VCTE examination (*n* 67), had unreliable VCTE results (*n* 507), reported significant alcohol consumption (i.e. > 2 drinks/d for women and > 3 drinks/d for men, *n* 106), were suffering from hepatitis B and/or C (*n* 83) or were taking steatogenic medications (i.e. amiodarone, valproate, methotrexate, tamoxifen and corticosteroid) for at least 3 months or more before study enrollment (*n* 74) were excluded[18,19]. A total of 3813 participants (1991 women and 1822 men) were included in the final analysis (online Supplementary Figure 1).

Dietary assessment

Dietary data including the clock time of all eating episodes (e.g. eating/drinking) were collected by trained interviewers through 24-h dietary recall. In order to enhance complete and accurate data collection and reduce respondent burden, the Automated Multiple-Pass Method was used in the NHANES. In the 2017–2018 cycle of the survey, participants completed the first 24-h dietary recall via face-to-face interview in a mobile examination center and completed the second 24-h dietary recall via telephone interview 3–10 d after the first recall. In our analysis, all participants (*n* 3813) had the first 24-h dietary recall and 53·9 % of participants (*n* 2056) completed two recalls.

In this study, TRE was defined as limiting usual intakes of food or beverage containing calories within 10 h in a day. Notably, TRE subjects included those who drunk zero energy beverages during the daily fasting period. Based on the time interval between first and last time of consuming food or beverage containing energy content in a day, early TRE (eating window between 05.00 and 15.00), late TRE (eating window between 11.00 and 21.00), long duration TRE (8–10 h eating window) and short duration TRE (≤ 8 h eating windows) were defined.

Assessment of covariates

Age, sex, race/ethnicity, education, marital status, family income, physical activity and smoking were collected by standardised questionnaires. Height, body weight and alcohol drinking were assessed through physical examination in the mobile examination center. The BMI was calculated as the weight (kg) divided by the square of height (m2). Economic status was measured as the ratio of family income:poverty which was calculated by dividing the total family income by the poverty threshold. Metabolic equivalent of tasks (METS)-hours/week was used to estimate the amount of physical activity. Healthy Eating Index-2015 (HEI-2015) score was used to reflect diet quality, which was described elsewhere[20]. Diabetes was defined according to

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self-reported a diagnosis of diabetes, HbA1c level ≥ 6·5 % or fasting plasma glucose level ≥ 126 mg/dl.

Ascertainment of non-alcoholic fatty liver disease

VCTE test was performed by technicians after a 2-day training program with an expert technician, using the FibroScan® model 502 V2 Touch equipped with a medium or extra-large probe. In line with previous studies[21,22], we used VCTE-derived controlled attenuation parameter to define NAFLD, with a cut-off value of median controlled attenuation parameter ≥ 274 dB/m. By comparing controlled attenuation parameter measurement for the detection of steatosis against biopsy, the area under the receiver operating characteristic curve was 0·87 (95 % CI: 0·82, 0·92) with a sensitivity and specificity of both 90 % for controlled attenuation parameter ≥ 274 dB/m among patients with NAFLD[21].

Statistical analysis

The standardised prevalence of NAFLD was calculated using the 2000 to 2025 WHO standard population (single ages to 79 and then 80 years or older). TRE was derived based on the first 24-h dietary recall in the analysis. We investigated TRE with different duration (8–10 and ≤ 8 h eating windows) and timing (early and late TRE) in relation to likelihood of NAFLD using logistic regression. We adjusted for age, sex, race/ethnicity, education, marital status, ratio of family income:poverty, physical activity, smoking, alcohol drinking, diabetes, BMI, total energy intake and HEI-2015 score. Selection of these covariates was based on the previously identified risk factors for NAFLD, professional knowledge and the observed incomparability of characteristics of participants (Table 1). For covariates with missing values, a separate missing indicator variable was created and included in the models. The trend tests were conducted using the median of each group of eating windows as a continuous variable. The heterogeneity between early and late TRE associated with NAFLD was tested using Cochran's Q test.

We also examined joint associations between hours of eating window and dietary quantity (indicated by total energy intake) and between hours of eating window and dietary quality (indicated by HEI-2015 score). Eating window was dichotomised into > 8 h and ≤ 8 h, and total energy intake and HEI-2015 score were dichotomised into two categories (low *v.* high) according to the median, resulting in four mutually exclusive groups (> 8 h-high, > 8 h-low, ≤ 8 h-high and ≤ 8 h-low). These four groups were then evaluated in relation to the likelihood of NAFLD in the logistic regression.

In sub-group analysis, we stratified the associations between TRE (≤ 8 h eating window) and NAFLD by age, sex, race/ethnicity, education level, marital status, family income:poverty ratio, smoking status, alcohol drinking, physical activity, BMI, diabetes, total energy intake and HEI-2015 score. We used the Wald test to examine whether the cross-product terms between these variables and exposures were statistically significant. In sensitivity analysis, we repeated the analysis in individuals who consistently reported the first and the last time of energy intake in the two 24-h recalls. All statistical tests were two-sided and performed using SAS (version 9.4, SAS Institute Inc).

Results

Characteristics of participants

Of the 3813 participants aged 18 years or older (mean age, 49·3 years; standard deviation (sd), 18·4 years), 1655 (age-standardised prevalence = 40·1 %) were diagnosed with NAFLD. The median eating window was 11·0 h (interquartile range: 9·0–12·5 h). Participants with short eating window (< 10 h) had lower prevalence of NAFLD, seemed younger, had a lower energy intake and HEI-2015 score, were less likely to be non-Hispanic whites and be married, had lower ratio of family income:poverty and were more likely to be current smokers (all $P < 0.05$, Table 1).

Time-restricted eating and non-alcoholic fatty liver disease

In general, the duration of eating window appeared to be directly associated with the prevalence of NAFLD (Table 2). After adjusting for age, sex, race/ethnicity, education, marital status, ratio of family income:poverty, physical activity, smoking, alcohol drinking, diabetes and BMI, participants with lower eating window (≤ 8 h) had lower likelihood of NAFLD with the OR of 0·71 (95 % CI: 0·53, 0·96, $P_{trend} = 0.008$), compared with those with eating window of no less than 10 h. When further adjusted for diet quantity (total energy intake) and quality (HEI-2015 score), such inverse association remained with the OR of 0·70 (95 % CI: 0·52, 0·93, $P_{trend} = 0.003$). TRE with 8–10 h of eating window also showed an inverse association with the odds of NAFLD, albeit weak and non-significant. No significant heterogeneity ($P_{heterogeneity} = 0.649$) was observed when investigated early (OR = 0·61, 95 % CI: 0·44–0·84) and late (OR = 0·73, 95 % CI: 0·36, 1·47) TRE in relation to NAFLD prevalence (Fig. 1).

When evaluated the joint association of hours of eating window and total energy intake, the association seemed strongest in the ≤ 8 h/low group with the OR for NAFLD of 0·55, 0·90, 0·97,1 (reference) for ≤ 8 h/low, ≤ 8 h/high, > 8 h/low and > 8 h/high, respectively. In the joint analysis of eating window and diet quality, the OR were 0·74 for ≤ 8 h/high, 0·63 for ≤ 8 h/low and 0·82 for > 8 h/high, compared with > 8 h/low group (Fig. 2).

Sub-group and sensitivity analyses

In sub-group analysis, we found that age ($P_{interaction} = 0.010$) and total energy intake ($P_{interaction} = 0.020$) may significantly modify the TRE-NAFLD association. The inverse association between TRE (eating window ≤ 8 h) and NAFLD appeared stronger in individuals who aged 65 years or younger compared with those over 65 years older and in individuals with lower total energy intake (below the median in the population) compared with those with higher energy intake (above the median). No differential associations were found according to physical activity, HEI-2015 or other factors (all *P* values for interaction were greater than 0·05, Fig. 3). In sensitivity analysis, the results were not essentially changed when we repeated the analysis in individuals who completed two 24-h dietary recalls (online Supplementary Table 1).

Table 1. Age-adjusted characteristics of participants according to daily eating window status in NHANES (2017–2018)*

Characteristic	Eating window ≥10 h %	Mean	SD	8–10 h %	Mean	SD	≤8 h %	Mean	SD	*P* value
Number of NAFLD cases (%)	45·2			39·3			39·9			0·006
Age, years		51·4	17·4		48·7	19·6		42·7	19·1	< 0·001
Female, %	51·9			57·6			50·8			0·048
BMI, kg/m^2		29·3	6·9		29·5	7·1		30·3	7·3	0·168
Total energy, kcal/d		2051	711		1896	722		1812	680	< 0·001
HEI-2015 score		53·9	14·1		51·9	13·7		50·3	13·7	< 0·001
Diabetes, %	18·1			19·5			22·3			0·422
Race/ethnicity, %										< 0·001
Non-Hispanic white	37·3			36·5			27·6			
Non-Hispanic black	19·0			20·5			34·0			
Other races	43·7			43·0			38·3			
Education, %										0·024
≤ 12th grade	17·8			16·3			19·3			
High school graduate	23·0			27·1			27·2			
More than high school	59·0			56·6			53·1			
Marital status, %										< 0·001
Married	61·3			54·6			47·7			
Widowed/divorced/separated	19·6			21·9			24·7			
Never married	15·0			18·3			20·5			
Ratio of family income to poverty										< 0·001
< 1·3	23·3			25·6			29·1			
1·3–3·5	34·8			40·1			36·0			
≥ 3·5	30·5			26·3			21·5			
Physical activity, METS-h/week										0·670
< 8·3	33·5			35·8			37·8			
8·3–16·7	9·7			9·7			9·4			
> 16·7	56·1			53·5			51·4			
Smoking, %										< 0·001
Never smokers	61·1			63·8			59·7			
Former smokers	24·2			23·8			21·6			
Current smokers	14·7			12·4			18·7			
Alcohol drinking, %										0·575
Never drinkers	11·0			10·5			10·9			
Former drinkers	18·3			21·4			23·1			
Current drinkers	67·8			66·8			63·5			

HEI-2015, healthy eating index-2015; METS, metabolic equivalent tasks; NAFLD, non-alcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey; SD, standard deviation.
* Variables were adjusted for age. Continuous variables were expressed as mean (SD) if normally distributed. Categorical variables were expressed as proportion (%). Values of polytomous variables may not sum to 100 % due to missing values or rounding.

Table 2. Association between daily eating window status and non-alcoholic fatty liver disease in NHANES (2017–2018)

	OR (95 % CI) ≥ 10 h	8–10 h OR	8–10 h 95 % CI	≤ 8 h OR	≤ 8 h 95 % CI	P_{trend}‖
No. of cases/participants	1160/2566	201/511		294/736		
Model 1*	Reference	0·89	0·60, 1·32	0·71	0·53, 0·96	0·008
Model 2†	Reference	0·90	0·60, 1·34	0·72	0·54, 0·97	0·012
Model 3‡	Reference	0·87	0·60, 1·27	0·69	0·51, 0·92	0·002
Model 4§	Reference	0·88	0·60, 1·29	0·70	0·52, 0·93	0·003

HEI-2015, healthy eating index-2015; METS, metabolic equivalent tasks; NHANES, National Health and Nutrition Examination Survey.
* Model 1 was adjusted for age (18–39, 40–59 and ≥ 60 years), sex (male, female), race/ethnicity (non-Hispanic white, non-Hispanic black and other races), education (≤ 12th grade, high school graduate and more than high school), marital status (married, widowed/divorced/separated and never married), ratio of family income:poverty (< 1·30, 1·30–3·49 and ≥ 3·50), physical activity (< 8·3, 8·3–16·7 and > 16·7 METS h/week), smoking (never smoking, former smoking and current smoking), alcohol drinking (never drinkers, former drinkers or current drinkers), diabetes (no, yes) and BMI (< 18·5, 18·5–24·9, 25·0–29·9 and ≥ 30·0 kg/m^2).
† Model 2: Model 1 + total energy intake (kcal/d, tertile).
‡ Model 3: Model 1 + HEI-2015 (score, tertile).
§ Model 4: Model 1 + total energy intake (kcal/d, tertile) + HEI-2015 (score, tertile).
‖ Linear trend test was conducted by assigning medians to each group as a continuous variable in the models.

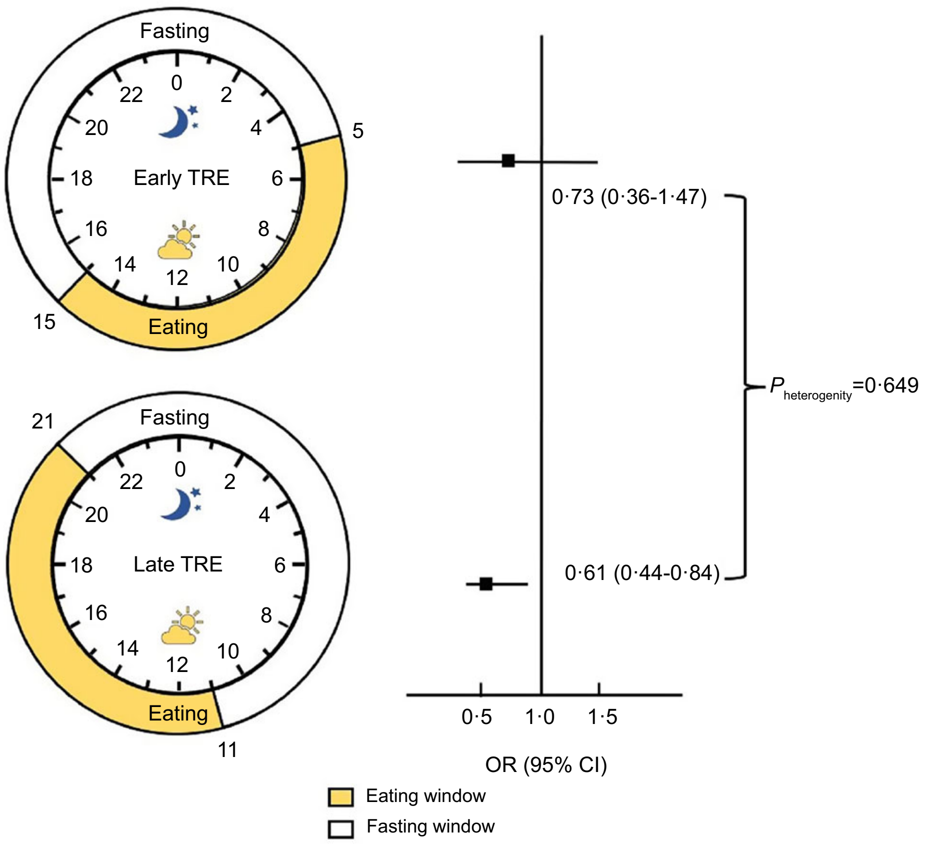

Fig. 1. Early and late time-restricted eating (TRE) and non-alcoholic fatty liver diseases in NHANES (2017–2018). NHANES, National Health and Nutrition Examination Survey. Early TRE, daily eating window during 05.00 and 15.00; Late TRE, daily eating window during 11.00 and 21.00. Covariates adjusted in the models were the same as those in model 4 in Table 2 (see Table 2 footnote). Heterogeneity analysis was performed between early TRE and late TRE using Cochran's Q test.

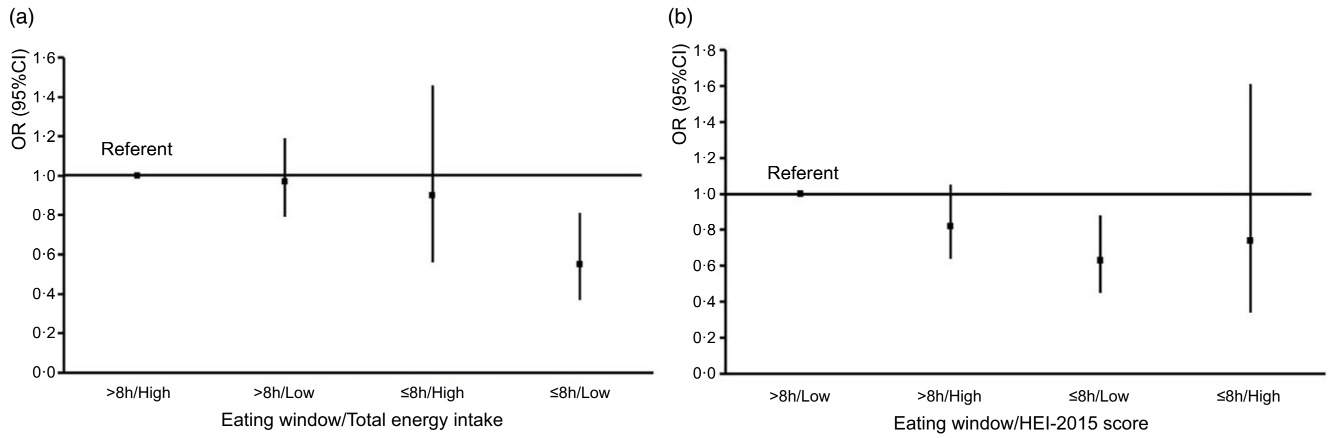

Fig. 2. Joint association of daily eating window and total energy intake (a)/HEI-2015 score (b) 1with odds of NAFLD. HEI-2015, healthy eating index-2015; NAFLD, non-alcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey. Eating window was dichotomised into > 8 h and ≤ 8 h, and total energy intake and HEI-2015 score were dichotomised into two parts according to the median (low and high), resulting in four mutually exclusive groups (i.e., > 8 h-high, > 8 h-low, ≤ 8 h-high and ≤ 8 h-low). These four groups were evaluated in relation to NAFLD risk using logistic regression. Covariates adjusted in the a and b were the same as those in model 3 and model 2 in Table 2 (see Table 2 footnote), respectively.

Discussion

In this nationally representative cross-sectional study of 3813 US adults, we found that TRE, particularly late TRE or TRE with short duration (i.e., eating window ≤ 8 h), was associated with lower odds of NAFLD. Moreover, such inverse association appeared stronger in persons with lower energy intake and was independent of physical activity and diet quality. To our knowledge, this is the first observational study to investigate TRE in relation to NAFLD in a free-living community-dwelling adult population. However, findings should be interpreted cautiously due to the

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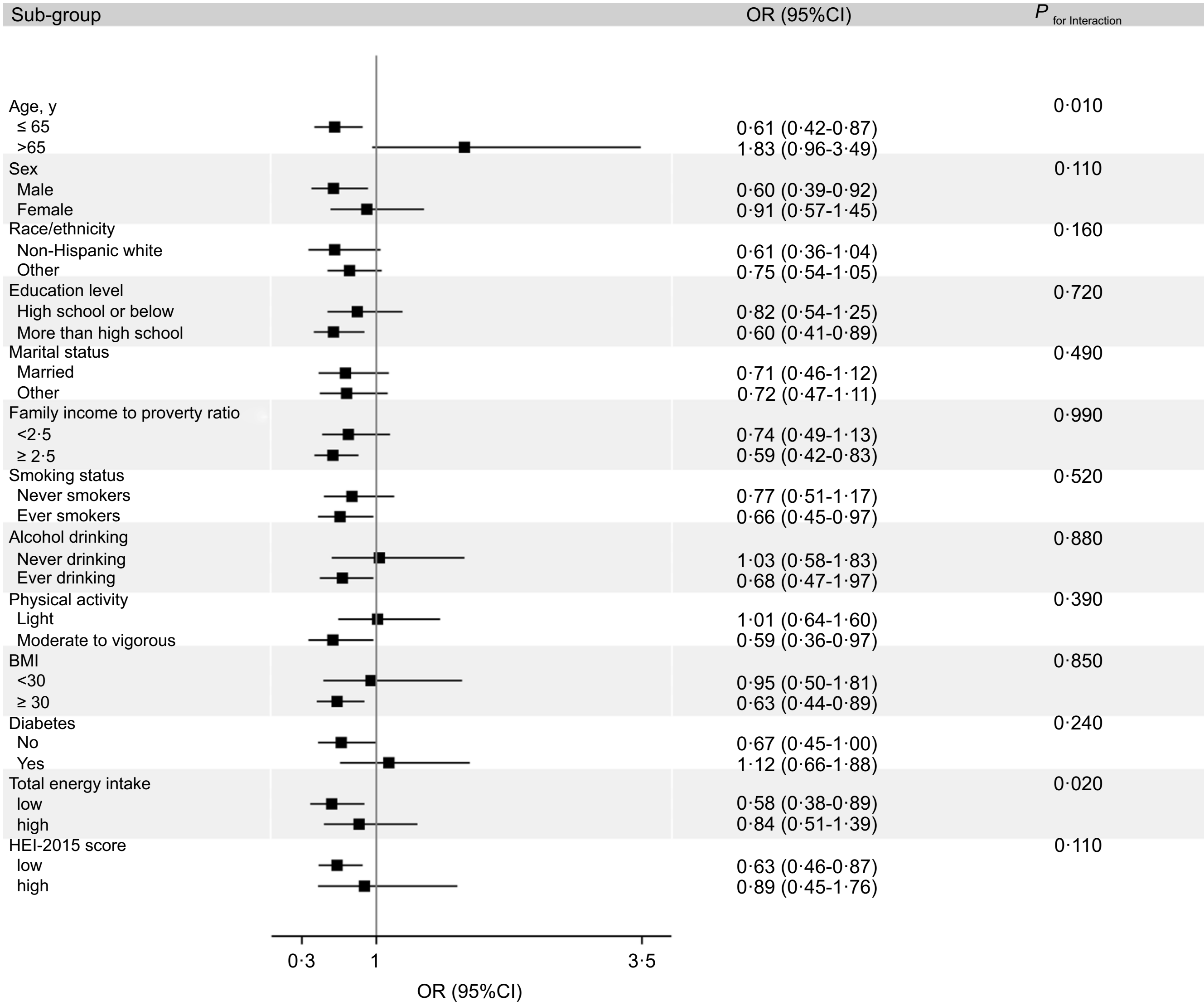

Fig. 3. Sub-group analysis on the association between time-restricted eating (eating window ≤ 8 h) and NAFLD in NHANES (2017–2018). METS, metabolic equivalent tasks; NAFLD, non-alcoholic fatty liver disease; NHANES, National Health and Nutrition Examination Survey. Covariates adjusted in the models were the same as those in model 4 in Table 2 (see Table 2 footnote). Of note, variables examined in this figure were not adjusted. Light physical activity was defined as participants with physical activity less than 8·3 METS-h per week, and moderate and vigorous activity was defined as participants who had physical activity of 8·3 METS-h per week or more. Total energy intake and HEI-2015 score were dichotomised into two parts according to the median: low and high.

potential misclassification of TRE based on one- or two-day recall of timing of eating occasions.

Previous studies of TRE and NAFLD are limited. The only clinical trial[12] showed that TRE (self-selected 10-h eating window) can reduce body weight and improve dyslipidaemia after 4–12 weeks among patients with NAFLD. Moreover, a short-term time-restricted feeding can decrease liver inflammation, albeit without significant weight loss or reductions in hepatic steatosis, in obese mice with NAFLD[23]. In addition to TRE, other IF forms including the ADF[11] and the 5:2[10] diet also showed beneficial to reduce body weight and liver steatosis among individuals with NAFLD after 8 weeks and 12 weeks, respectively. There are several plausible biological mechanisms to explain the association between TRE and NAFLD. First, it has been well documented that TRE was conducive to reduce body weight and fat mass in diverse populations[24,25]. In the clinical practice guideline, lifestyle-induced weight loss by dietary management is recommended as one of the initial interventions of NAFLD[26]. Second, in previous studies, TRE was reported to be associated with reduced fasting glucose and improved insulin sensitivity and lipid metabolism[27–29], which play an essential role in the occurrence and progression of NAFLD[30,31]. Third, the circadian clock, which may be altered by mealtime[32], participates in the regulation of hepatic TAG accumulation, oxidative stress, inflammation and mitochondrial dysfunction[33–35], which can lead to the advanced form of NAFLD (i.e. non-alcoholic steatohepatitis)[36]. Thus, TRE may prevent or improve NAFLD partly by weight loss, metabolic regulation and mitigating circadian

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rhythms disruption. The current study adds more evidence that following TRE may prevent the likelihood of NAFLD in free-living individuals.

We observed that TRE with long and short hours of eating window both showed an inverse with the odds of NAFLD. Consistent with our results, TRE with eating window ≤ 8 h (e.g., 4 h[28], 6 h[28,32] and 8 h[12,27]) showed benefit effects on weight loss, reduction fasting glucose, improving insulin sensitivity and lipid metabolism, amelioration inflammation or increase gut microbial diversity in overweight, obesity and NAFLD patients after a period of intervention. Similarly, 8–10 h eating window (e.g. 8–9 h[37] and 10 h[38]) of TRE might be beneficial for reducing waist circumference, lowering blood pressure or weight loss in patients with abdominal obesity and metabolic syndrome, compared with no-intervention control groups. Taken together, the health effects of the TRE duration vary from study to study, therefore more studies with larger sample sizes are warranted to determine the most suitable duration of TRE on health effects.

We found no difference in the associations of early and late TRE with NAFLD. How the exact timing of TRE (early *v.* late TRE) effects health remains unclear. Previous study[27] suggested that 8 h early TRE (06.00–15.00) could improve insulin sensitivity, reduce blood pressure and reduce body mass in healthy volunteers. While an randomised controlled trial (RCT)[28] in adults with obesity showed beneficial effects of 6 h late TRE (13.00–19.00) to reduce body weight, insulin resistance and oxidative stress. In addition, evidence from another study[14] found that early (08.00–18.00) and late (00.00–21.00) TRE had no significant difference in weight loss between the two groups, which was partly consistent with our results. Although the results appeared stronger for late TRE, there was no statistical difference between the two groups. Therefore, the association between TRE and NAFLD did not differ according to the timing during different periods of the day. The above discrepancies could be possibly due to differences in the eating window, study population, sample size and intervention duration. Further clinical trials or cohort studies are needed to investigate the health effects in these areas.

We showed that the inverse association between TRE and NAFLD was stronger in participants with lower energy intake. In a clinical trial[29], similar effects in reducing weight, body fat, liver fat, blood pressure, glucose levels and lipid levels were found both in energy restriction with TRE group and only daily calorie restriction group over a 12-month intervention period, which indicated that most of the beneficial effects of TRE could be explained by energy intake restriction. However, diet quality and physical activity appeared not to significantly modify the TRE-NAFLD association. A meta-analysis suggested that IF had an independent benefit on weight loss and improvement of liver function in patients with NAFLD because there were no exercise or other interventions in these studies included in the meta-analysis[39]. In addition, this inverse association was stronger in young participants. However, the underlying mechanism for potential age difference remains unclear and needs to be elucidated in future research. Alternatively, the difference could be due to chance.

Our study has several strengths, including large sample size, a nationally representative sample of US adults and a reliable VCTE detection to diagnose NAFLD. The biggest limitation to this study is that the timing of food intake was derived based on one- or two-day recall, which may not well capture the long-term eating habits, and lead to a serious misclassification bias. Nonetheless, about 10 % of US adults habitually maintain a daily fasting for ≥ 12 h[16], which enable the feasibility to investigate TRE patterns in observational studies. Furthermore, a recent validation study showed the modest agreements between food times derived from a recall-based survey and food times estimated from multiple-day food records[40]. In addition, measurement errors in self-reports of other lifestyle factors may exist. Also, the cross-sectional design in the current study is not strong enough to demonstrate causality.

In summary, our study found that TRE (≤ 8 h eating window) was associated with lower likelihood of NAFLD. This protective association seemed stronger in young adults and in individuals who consumed less energy. Prospective cohort studies to investigate the association between TRE adherence and the long-term risk of NAFLD are warranted. In addition, the difficulty of how best to measure the habitual timing of food intake in epidemiological studies needs to be solved urgently.

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Supplementary material

For supplementary material/s referred to in this article, please visit https://doi.org/10.1017/S0007114523000818

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