The Association of the Consumption Time for Different Food with the Cardiovascular Disease and All-Cause Mortality Among Diabetes Patients

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Abstract

Background:

This study aims to investigate whether food consumed time and distribution at three-meals is associated with long-term survival among the people with diabetes.

Methods:

This study included 4,699 diabetes patients participating in the National Health and Nutrition Examination Survey from 2003 to 2014. Food consumed across a day including the forenoon, afternoon, evening, were divided into quantiles based on their distribution. Cox proportional hazards regression models were used to analyze the survival relationship between food intakes time and distribution (with a constant quality and quantity) and mortality.

Results:

After adjustment for multiple covariates, in the forenoon, compared to the participants with diabetes in the lowest consumption quantile of potato and starchy-vegetable, participants with diabetes in the highest consumption quantile had lower mortality risk of CVD(HR_{potato}=0.52, 95%CI: 0.38-0.87; $HR_{starchy\text{-}vegetable}$= 0.51, 95%CI: 0.29-0.90). In the evening, the highest quantile of dark-vegetable intake is related to lower mortality risk of CVD(HR=0.64, 95%CI: 0.45-0.92) and all-cause(HR=0.81, 95%CI: 0.66-0.99), whereas participants in the highest quantile of intakes of refined grain and processed meat are more likely to die due to CVD($HR_{refined\text{-}grain}$=1.54, 95%CI:1.10-2.15; $HR_{processed\text{-}meat}$=1.83, 95%CI:1.20-2.77) and all-cause($HR_{refined\text{-}grain}$=1.29, 95%CI:1.01-1.65; $HR_{processed\text{-}meat}$=1.37, 95%CI:1.06-1.75). Iso-calorically switching 0.1 serving refined grain or processed meat consumed in the evening to the forenoon, and 0.1 serving dark vegetable consumed in the afternoon to the evening reduced the risk of CVD mortality.

Conclusions:

Higher intake of potato, starchy-vegetable in forenoon, dark-vegetable in the evening, and lower intake of refined-grain and processed-meat in the evening was associated with better long-term survival in people with diabetes.

Background

Diet is an accepted modifiable behavior that could be helpful for the prevention and therapy of diabetes [1]. Previous studies frequently focused on the health impact of the quantity and quality of different foods or nutrients on the management of diabetes. However, in recent years, overwhelming animal studies have demonstrated that the ingestion time is another major factor for the well-being of organisms because of the circadian effects [2–5]. Meanwhile, accumulating human studies also found that breakfast skipping, high frequency of eating in a day, higher energy intake at dinner, and late-night eating are associated with higher inflammation levels, poorer cardio-metabolic health and greater incidence of obesity and type 2 diabetes [6–11]. Additionally, our recent study also found that the consumption model of higher energy at breakfast with lower energy at dinner was associated with a better long-term survival among people with diabetes [12].

Although the above evidence has suggested that the time of ingestion plays an important role in the prevention and treatment of diabetes, few studies have examined the association of consumption time of different food (especially distribution of food consumption across a day under a constant quality and quantity) with the nature course of diabetes. Therefore, based on current evidence, we hypothesis that different food might have different optimal consumption time for people with diabetes, and it may aid in helping the people with diabetes to select appropriate food at optimal time, thereby improving the nutritional management by understanding the association between consumption time of different food and long-term survival. Based on the data from the National Health and Nutrition Examination Survey (NHANES), this study aims to examine the association of different food groups consumed at different time and consumed distribution with cardiovascular disease (CVD) and all-cause mortality in people with diabetes.

Methods

Study population

As a stratified and multistage study, NHANES is designed by National Center for Health Statistics (NCHS). A nationally representative sample of the non-institutionalized civilian population of the U.S. was investigated to assess the health and nutritional status. The detailed introduction about NHANES has been described elsewhere[13]. This study recruited people aged over 18 years with diabetes who participated in the NHANES during 2003-2014. Diabetes was defined by the following any criteria: 1) self-reported information, 2) fasting plasma glucose level (FPG) > 7.0 mmol/l, 3) hemoglobin A1c level (HA1c) > 6.5%. After excluding participants with diabetes who had 1) missing or unknown information on any dietary nutrient intake, 2) missing information of mortality. Finally, 4699 participants with diabetes (2413 men and 2286 women) were included. Research Ethics Review Board of National Center for Health Statistics approved NHANES, and all participants with diabetes had already provided written informed consent before initial exam. The NHANES data could be accessed through https://wwwn.cdc.gov/nchs/nhane.

Dietary assessment

Information about food intakes for two non-consecutive days were collected through 24-hour dietary recall interviews. In the first one, the dietary investigation was conducted in-person, and in the other one, the dietary investigation was conducted 3–10 days afterwards by calling. According to the United States Department of Agriculture's Food and Nutrient Database for Dietary Studies, the individual energy and nutrient intake was estimated. In line with the MyPyramid Equivalents Database 2.0 for USDA Survey

Foods (MPED 2.0), dietary food consumption of participants with diabetes in the NHANES was also integrated into 18 definable MyPyramid major food groups.

Main exposure

Align with the consumption time, we split the major food groups intake into different period, such as the forenoon (breakfast plus snack between breakfast and lunch), the afternoon (lunch plus snack between lunch and dinner), the evening (dinner plus snack after dinner).

Main outcome

In this research, the status of CVD and all-cause mortality was the major outcome variable. The mortality status was determined by the National Death Index (NDI) until 31 December 2015. The NDI is a highly reliable resource, which has been widely used for death identification. As an international disease classification method, the ICD-10 is used for the determination of disease-specific death. The ICD-10 codes I00–I09, I11, I13, I20–I51, or I60–I69 was defined as CVD mortality. In total, this study documented 913 deaths, including 314 deaths due to CVD death.

Assessment of covariates

Non-dietary covariates were sex (male/female), age (years), BMI (kg/m2), drink (yes/no), smoke (yes/no), regular exercise (yes/no), education (less than 9^{th} grade, between 9^{th} and 11^{th} grade, graduate from high school, GED or equivalent, Arts degree of some college or Associate, college graduate or above), race/ethnicity (non-Hispanic white/non-Hispanic black/Mexican American/other), household income per year (<$20,000, $20,000–$45,000, $45,000–$75,000, or >$100,000), family history of diabetes (yes/no), diagnosis record of hypertension or dyslipidemia (yes/no), drug use for controlling blood pressure, cholesterol and glucose. And the dietary covariates included total intakes of energy (kcal/day), carbohydrate (g/d), dietary fat (g/day), protein (g/day), major food groups and Alternate Healthy Eating Index (AHEI), which is an indicator of dietary quality.

Statistical analysis

All analyses were performed according to the guidelines analytic of NHANES. Continuous variables about demographic characteristics, anthropometric measurements, and dietary nutrient and food intakes, were showed as mean (SD) or median (P25, P75); whereas, categorical variables were showed as number (percentage). General linear models adjusting for age and x^2 tests were used to compare baseline characteristics by mortality status. All statistical analyses were conducted by R 4.0.2, and two-sided $P < 0.05$ was considered to be statistically significant.

Cox proportional hazards models

Food groups consumed in forenoon, afternoon, and evening were transformed into categorical variables based on their distribution, respectively. Cox proportional hazards (CPH) models were performed to estimate the hazards ratio(HR) and 95% confidence interval (CI) for the association of food consumed in the forenoon, afternoon and evening with CVD and all-cause mortality. Follow-up years of participants with diabetes between interview date and death or census date (31 December 2015) was defined as Survival time. A series of covariates was also controlled, which were including age, sex, ethnics, education, income, smoking, drinking, regular exercise habits, BMI, total intake of daily energy, fat, carbohydrate, protein, family history of diabetes, hypertension and dyslipidemia, and medication. Moreover, when analyzing one food group consumed in one time period across a day, we also controlled the total intake of this food group in the whole day.

Predicted isocaloric models

Based on the CPH model developed in previous steps, we also built several isocaloric models to evaluate relative risk of deaths with altered distribution of food consumption time, which was conducted via one food group consumed at one time period theoretically replacing with the equivalent food group consumed at another time period[12]. A key rationale of the substitution analysis is that, in the isocaloric setting, the total intake of energy, macronutrients and the food group are held constant.

Sensitivity analysis

We performed three kinds of sensitivity analyses. In the first analysis, we excluded the diabetes patients, whose survival time less than two years or follow-up duration less than two years to examine the impact of severe illness or accident on the results. In the second analysis, the indicator of overall dietary quality and breakfast skipping were additionally adjusted in the CPH model to evaluate whether these confounders would influence the results.

Results

Baseline characteristics

In terms of CVD mortality status, the baseline characteristics of demographic information, anthropometric results, nutrition intakes, are showed in Table 1. Compared to diabetes patients who not died and died of non-CVD, patients with CVD mortality were more likely to be men, non-Hispanic white, had higher age, prevalence of hypertension, and had lower BMI, education level, family annual income, diet quality, energy and macronutrient intake (P<0.05).

Mortality

Among the 18 major food groups, the intake distribution of potato, starchy vegetable, dark vegetable, refined grain and processed meat at different time periods across a day were observed to be related to the mortality risk of CVD and all-cause. As shown in Figure 1, compared to the participants with diabetes in the lowest quantile of intakes of refined grain, potato and starchy vegetable in the forenoon, participants with diabetes in the highest quantile had lower mortality risk of CVD ($HR_{\text{refined grain}}$ = 0.68, 95%CI: 0.49-

0.92; HR_{potato} = 0.52, 95%CI: 0.32-0.87; $HR_{starchy\ vegetable}$ = 0.51, 95%CI: 0.29-0.90), all-cause ($HR_{refined\ grain}$ = 0.72, 95%CI: 0.57-0.91). In the evening, the higher intake of refined grain or processed meat was associated with a higher probability of deaths due to CVD and all-cause. The HR indicated participants with diabetes who were in the highest quantile were more likely to die due to CVD ($HR_{refined\ grain}$ =1.54, 95%CI: 1.10-2.15; $HR_{processed\ meat}$ =1.83, 95%CI: 1.20-2.77) and all-cause ($HR_{refined\ grain}$ =1.29, 95%CI: 1.01-1.65; $HR_{processed\ meat}$ =1.37, 95%CI: 1.06-1.75). Moreover, compared to the participants with diabetes in the lowest quantile of dark vegetable intake in the evening, participants with diabetes in the highest quantile had lower mortality risk of CVD ($HR_{dark\ vegetable}$ = 0.64, 95%CI: 0.45-0.92), all-cause ($HR_{dark\ vegetable}$= 0.81, 95%CI: 0.66-0.99). Additionally, no significant association between the intakes of other food groups at different time periods within a day and mortality risk was observed, which were presented in Supplementary Table A to C.

Isocaloric substitution analysis

Because the intakes of refined grain, potato, starchy vegetable in the forenoon, and the intakes of dark vegetable, refined grain and processed meat in the evening were associated with CVD mortality. To examine the association of changed distribution of diet food intake with CVD death risk, the isocaloric substitution analyses were therefore performed to examine whether switching these food groups consumed at different time points would modify the mortality risk. Figure 1 showed that the HR of CVD mortality decreased by 2% ($HR_{refined\ grain}$ =0.98, 95%CI: 0.97-0.99) when 0.1 serving refined grain consumed in the evening was iso-calorically switched to the refined grain consumed in the forenoon. Similarly, the HR of CVD mortality decreased by 1% ($HR_{processed\ meat}$ =0.99, 95%CI: 0.98-0.99) when 0.1 serving processed meat consumed in the evening was iso-calorically replaced by the same serving consumption in the forenoon. Meanwhile, the HR of CVD mortality decreased by 9% ($HR_{dark\ vegetable}$=0.91, 95%CI: 0.85-0.97) when 0.1 serving dark vegetable consumed in the evening was used to iso-calorically replace the same serving consumption in the afternoon.

Sensitivity Analysis

In the first sensitivity analysis, after the exclusion of participants with diabetes who died within two years of follow-up or had follow-up duration of less than two years, the negative association of higher intake of potato in the forenoon and higher intake of dark vegetable in the evening with lower CVD and all-cause mortality was still significant, and the positive association of higher intake of refined-grain, processed meat with greater CVD and all-cause mortality was also significant (Supplementary Table D). These results indicated the above association was not affected by the severe illness. Moreover, results of second sensitivity analysis supported that after additionally adjusting for the confounders of dietary quality and breakfast skipping in the CPH models, most of the relationships between food groups and CVD and all-cause mortality (except refined grain in forenoon) were robust significant, which suggested that the overall dietary quality and breakfast skipping hardly influence the results (Supplementary Table E and F).

In these three sensitivity analysis, the HR of CVD mortality was decreased (Supplementary Figure1-3) when changing distribution of consumption time for refined grain (from evening to forenoon), processed meat(from evening to forenoon and afternoon), and dark vegetables(from evening to afternoon). These results supported the distribution of consumption time for diet food groups could impact the CVD mortality risk.

Discussion

Our study demonstrated that diabetes patients with more potato and starchy-vegetable consumption in the forenoon and dark-vegetable in the evening had lower mortality risk of CVD and all-cause; however, diabetes patients with more refined grain and processed meat consumption in the evening had a greater mortality risk of CVD and all-cause. Further, under a constant quality and quantity, iso-calorically switching 0.1 serving intake of refined grain or processed meat consumption from the evening to the forenoon, and 0.1 serving intake of dark vegetable from the afternoon to the evening could significantly reduce the risk of CVD-mortality.

We firstly examined the association between different food groups consumed at different time and the long-term survival among people with diabetes. Therefore, the most finding of our study was that food groups including potato, starchy-vegetable, dark vegetable, refined grain and processed, had optimal consumption time for decreasing the risk of CVD mortality among people with diabetes, which were independent of the nutritional confounders. It has been documented that the carbohydrate metabolism including the hepatic and peripheral insulin sensitivity, and the secretion of insulin have biological rhythm, which are in high levels in the forenoon, and gradually decrease from day to night [14]. The potato and starchy-vegetable contain high amount of carbohydrate [15], therefore, the fluctuation of glucose after higher intakes of them in the forenoon are likely more accordance with the biological rhythm of insulin sensitivity, probably aiding in the glucose control, which is a possible reason for explaining their beneficial effect in the forenoon among people with diabetes. Moreover, the recent study demonstrated that people with diabetes had disrupt expression of clock gene, REV-ERB-α and REV-ERB-β in the peripheral tissue [16], and evidence have found that higher energy intake during the active period could reverse the disrupted clock gene expression [10, 17–19]. Another human study found that the three-meal diet with a carbohydrate-rich breakfast would up-regulate clock gene expression, leading to weight loss and maintain a good glycemic level allow in diabetes patients [11]. All above research further support the beneficial effect of high intakes of potato, starchy-vegetable in the forenoon on the long-term survival among people with diabetes.

Moreover, although the beneficial effect of dark vegetable consumption on the glucose control among people with diabetes has been abundantly demonstrated in previous studies [20–22], it is still largely unknown whether there is an optimal intake time of dark vegetable for diabetes. This study suggested that its optimal ingestion time might be in the evening. Iso-calorically substitution model result displayed that 0.1 serving dark vegetable intake switched from the afternoon to the evening could significantly reduce the risk of CVD mortality under a constant daily dark vegetable intake. Our recent study has demonstrated that vegetable dietary pattern in evening was related to low mortality risk of CVD and all-cause in general population, further supporting the results of this study [23]. In diabetes patients, the progression of microvascular disorder interferes with the normal nocturnal blood pressure decline in the evening, and induce a persistently increased pulse pressure, which further contributes to their raised cardiovascular risk [24–25]. Thus, the vegetable consumed distribution with a high intake at night might improve the increased blood pressure in evening for diabetes patients. And the low energy intake is another possible mechanism for such beneficial effect. Abundant studies have illustrated that the low energy intake in evening had improving effects on cardiometabolic health and long-term survival. The low-energy food was a lower inflammatory index food, consumed in evening is likely to reduce the stream pro-inflammation cytokines (peak at nigh) of organism [26–27], so as to prevent cardiovascular disease. In addition, it has been reported that gut microbes have their internal circadian pattern [28–29]. The relative abundance of bacteria producing short-chain fatty acids is frequently highest at night, and then tend to decrease in daytime [30]. Hence, intaking more dark vegetable in the evening is align with amount rhythm of that kind bacteria, which stimulate them to generate much more short-chain fatty acids, and accordingly promotes nutritional metabolic processing [31–32].

Further, we also observed that participants with diabetes who consumed the refined grain and processed meat in the evening were more likely to die due to CVD and all-cause. Generally, higher intakes of them in the evening are usually related to higher energy intake. In contrast to the beneficial effect of refined grain consumed in the forenoon, higher intake of them in the evening is likely contradictory to the biological rhythm of insulin sensitivity and secretion, probably resulting in the poorer glucose control among people with diabetes. Processed meat contains relative high amount of saturated fatty acids and protein [33–34]. The previous study has indicated that higher intake of saturated fatty acids and animal protein at dinner is associated with CVD and all-cause mortality, which may support the harmful effects of processed meat consumed in the evening on the long-term survival among people with diabetes [12]. Additionally, higher intake of processed meat is frequently related to higher inflammation levels [35]. Therefore, higher intake of processed meat in the evening may further increase the inflammation level at night. A previous animal research reported that the later intake of saturated, the worse pro-inflammation cytokines circadian patterns, which aggravates the chronic low inflammation state [36].

The findings in our study have important implications. In recent years, due to the people with diabetes are under a disrupted biological rhythm of glucose metabolism, accumulating evidence has indicated that food intake time is as important as quantity and quality for maintaining health. Therefore, the nutritional therapy with considering the consumption time will be a major component of diabetes treatment. Based on the results in this study, we believed that people with diabetes might largely decrease their mortality risk of CVD by choosing consumption time for the specific food. This information provides an opportunity for individualized nutritional therapy plans for patients with diabetes. Certain limitations also presence in our study. First, self-reported 24-h dietary recall was used instrument to collect diet information. Although it is a common method in observational studies, the measurement error still exits due to the day-to-day variations in food intake. Second, some unmeasured confounding factors is hard to control. Third, this study was not able to distinguish different types of diabetes. Future studies are needed to examine this association in terms of type 1 and type 2 diabetes in order to provide more comprehensive evidence.

Conclusions

In this study, we suggested that diabetes should intake more potato and starchy-vegetable in the forenoon and dark-vegetable in the evening, as well as less refined-grain and processed-meat in the evening, which was associated with better long-term survival.

Abbreviations

NHANES
National Health and Nutrition Examination Survey; HR:hazards ratio; CI:confidence interval; CVD:cardiovascular disease; NCHS:National Center for Health Statistics ; FPG:fasting plasma glucose level; HA1c:hemoglobin A1c level; MPED:MyPyramid Equivalents Database; NDI:National Death Index; CPH:Cox proportional hazards.

Declarations

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Authors' Contributions

YL and TS.H designed this study. WW and WB.J carried out the statistical analysis. QR.S, JZ and YY.C repeated the analysis. WW wrote and reported the manuscript. WB.J and CH.S revised this manuscript. All authors critically assessed and reviewed the paper and approved the version to be published. TS.H is the guarantor of this work.

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Availability of data and materials

The data in this study are available from website https://wwwn.cdc.gov/nchs/nhane.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

There is no competing interests with this manuscript.

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Tables

Table-1 Baseline characteristics in terms of CVD mortality status

	CVD mortality (n=314)	Non-CVD mortality (n=4385)	P value
Age，years	70.20 (10.59)	60.49(13.862)	0.000
Female,%	132(42.04)	2154(49.12)	0.015
Non-Hispanic white,%	159(50.64)	1634(37.26)	0.000
Current smoking,%	55(17.52)	844(19.25)	0.462
Current drinking,%	173(55.10)	2613(59.59)	0.268
College graduate or above,%	24(7.64)	621(14.16)	0.000
≥$100,000 annual household income,%	6(1.91)	299(6.82)	0.000
BMI,kg/m^2	29.00 (8.72)	31.99 (8.08)	0.001
Regular exercise,%	55(17.52)	705(16.08)	0.696
Total energy，kcal/day	1573.4 (591.70)	1816.8 (773.52)	0.001
Total protein,g/d	67.10 (28.08)	75.67 (34.38)	0.008
Total carbohydrate,g/d	189.68 (74.08)	217.09 (96.07)	0.004
Total fat,g/d	59.82 (28.15)	70.84 (37.26)	0.001
Family history of diabetes,%	0(0.00)	130(2.96)	0.002
Ever controlled diabetes,%	269(85.67)	3737(85.22)	0.829
Prevalent hypertension,%	250(79.62)	3162(72.11)	0.004
Ever controlled hypertension,%	215(68.47)	2578(58.79)	0.001
Prevalent dyslipidemia,%	173(55.10)	2421(55.22)	0.968
Ever controlled dyslipidemia,%	166(52.87)	2171(49.51)	0.389
Whole grain (Ounce equivalents)	0.52 (0.00-1.21)	0.49(0.00-1.24)	0.934
Refined grain (Ounce equivalents)	3.96(2.61-5.68)	4.66(3.05-6.65)	0.000
Red and orange vegetable (Cup equivalents)	0.14(0.00-0.42)	0.26(0.070.56)	0.000
Potato (Cup equivalents)	0.18(0.00-0.56)	0.20(0.00-0.54)	0.342
Starchy vegetable (Cup equivalents)	0.11(0.00-0.57)	0.28(0.00-0.70)	0.000
Tomato (Cup equivalents)	0.12(0.00-0.34)	0.17(0.03-0.39)	0.001
Fruit (Cup equivalents)	0.01(0.00-0.36)	0.00(0.00-0.24)	0.001

Milk (Cup equivalents)	0.57(0.12-1.13)	0.47(0.13-1.03)	0.207
Cheese (Cup equivalents)	0.11(0.00-0.46)	0.27(0.00-0.73)	0.000
Red meat (Ounce equivalents)	1.08(0.00-2.40)	1.02(0.00-2.36)	0.689
Poultry (Ounce equivalents)	0.14(0.00-1.60)	0.78(0.00-2.15)	0.000
Eggs (Ounce equivalents)	0.21(0.02-0.90)	0.29(0.03-0.95)	0.077
Soy (Ounce equivalents)	0.00(0.00-0.00)	0.00(0.00-0.00)	0.027
Processed meat (Ounce equivalents)	4.31(2.61-6.82)	4.89(2.96-7.52)	0.017
Yogurt (Yes/No), %	25(7.06%)	455(10.38%)	0.172
Dark vegetable (Yes/No), %	87(27.7%)	1471(33.5%)	0.034
Seafood (Yes/No), %	91(29.0%)	1358(31.0%)	0.461
Legumes (Yes/No), %	85(27.1%)	1432(32.7%)	0.041

Continuous variables are presented as mean (SD) or median (P25, P75), and Categorical variables are presented as Number (percentage).

Table 2-adjusted HRs for the refined grain, dark vegetable, potato, starchy vegetable and processed meat consumed in the forenoon and evening and CVD-mortality and all-cause mortality

	CVD mortality		All-cause mortality	
	Case/N	HR (95%CI)	Case/N	HR (95%CI)
In the forenoon				
Refined grain (Quartiles)				
Q1	79/990	1	206/990	1
Q2	90/1263	0.70 (0.47-1.05)	268/1263	0.78 (0.65-0.94)
Q3	94/1351	0.71 (0.52-0.98)	287/1351	0.81 (0.67-0.98)
Q4	51/1095	0.68 (0.49-0.92)	152/1095	0.72 (0.57-0.91)
P for trend		0.079		0.012
$P_{\text{interaction with sex}}$		0.545		0.381
Dark vegetable (Yes/No)				
No	309/4562	1	895/4562	1
Yes	5/137	0.68 (0.27-1.69)	18/137	0.95 (0.59-1.54)
P for trend		0.407		0.840
$P_{\text{interaction with sex}}$		0.841		0.553
Potato (Yes/No)				
No	297/4186	1	836/4186	1
Yes	17/513	0.52 (0.32-0.87)	77/513	0.88 (0.69-1.13)
P for trend		0.013		0.326
$P_{\text{interaction with sex}}$		0.171		0.384
Starchy vegetable				
No	301/4174	1	852/4174	1
Yes	13/525	0.51 (0.29-0.90)	61/525	0.83 (0.63-1.10)
P for trend		0.020		0.193
$P_{\text{interaction with sex}}$		0.525		0.552
Processed Meat (Tertiles)				
T1	212/2818	1	610/2818	1
T2	42/616	0.89 (0.63-1.26)	110/616	0.82 (0.66-1.01)
T3	60/1265	0.77 (0.56-1.05)	193/1265	0.88 (0.74-1.06)

P for trend		0.089		0.093
$P_{\text{interaction with sex}}$		0.433		0.844
In the evening				
Refined grain (Quartiles)				
Q1	73/1031	1	211/1031	1
Q2	89/1334	1.09 (0.79-1.50)	270/1334	1.08 (0.90-1.30)
Q3	51/1049	1.40 (0.90-2.16)	171/1049	1.19 (0.98-1.46)
Q4	101/1285	1.54 (1.10-2.15)	261/1285	1.29 (1.01-1.65)
P for trend		0.023		0.029
$P_{\text{interaction with sex}}$		0.997		0.493
Dark vegetable (Yes/No)				
No	263/3653	1	746/3653	1
Yes	51/1046	0.64 (0.45-0.92)	167/1046	0.81 (0.66-0.99)
P for trend		0.015		0.046
$P_{\text{interaction with sex}}$		0.252		0.281
Potato (Tertiles)				
T1	176/2664	1	502/2664	1
T2	49/750	0.86 (0.63-1.20)	161/750	0.97 (0.81-1.17)
T3	89/1285	0.88 (0.63-1.24)	250/1285	0.86 (0.70-1.04)
P for trend		0.401		0.148
$P_{\text{interaction with sex}}$		0.661		0.957
Starchy vegetable(Tertiles)				
T1	176/2380	1	491/2380	1
T2	54/980	0.78 (0.57-1.06)	187/980	0.94 (0.79-1.12)
T3	84/1339	0.96 (0.67-1.36)	235/1339	0.88 (0.71-1.08)
P for trend		0.503		0.195
$P_{\text{interaction with sex}}$		0.183		0.093
Processed meat (Quartiles)				

Q1	67/1049	1	209/1049	1
Q2	83/1258	1.14 (0.82-1.58)	262/1258	1.11 (0.92-1.34)
Q3	81/1278	1.21 (0.85-1.73)	232/1278	1.07 (0.87-1.31)
Q4	83/1114	1.83 (1.20-2.77)	210/1114	1.37 (1.06-1.75)
P for trend		0.009		0.043
$P_{\text{interaction with sex}}$		0.583		0.996

Data are HRs and (95%CI), and confounders included age, sex, ethnics, education, income, smoking, drinking, regular exercise habits, BMI, total intake of daily energy, fat, carbohydrate, protein, family history of diabetes, hypertension and dyslipidemia, and medication, total intake of specific food group in a day. Case/N, mortality number/total number.

Figures

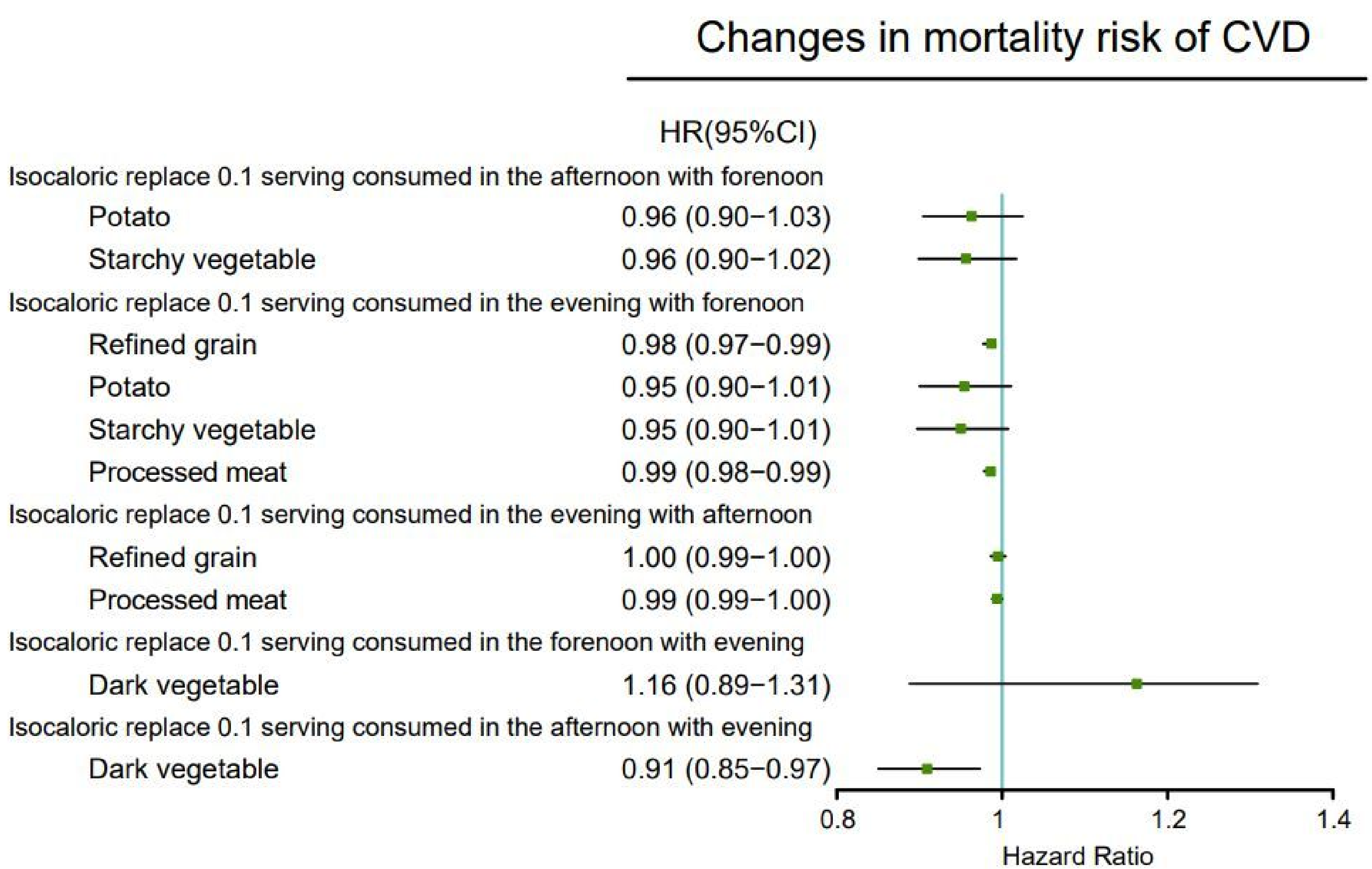

Figure 1

Adjusted HR for CVD mortality: isocaloric substitution of refined grain, potato, starchy vegetable or processed meat consumed in the evening to the forenoon, and isocaloric substitution of dark vegetable consumed in the forenoon or afternoon to the evening. Adjustments included age, sex, ethnics, education, income, smoking, drinking, regular exercise habits, BMI, total intake of daily energy, fat, carbohydrate, protein, family history of diabetes, hypertension and dyslipidemia, and medication, total intake of specific food group in a day. Case/N, mortality number/total number.

Supplementary Files

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