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Frequency of eating and concentrations of serum cholesterol in the Norfolk population of the European prospective investigation into cancer (EPIC-Norfolk): cross sectional study

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Abstract

Objectives To examine the relation between self reported eating frequency and serum lipid concentrations in a free living population.
Design Cross sectional population based study.
Setting Norfolk, England.
Participants 14 666 men and women aged 45-75 years from the Norfolk cohort of the European prospective investigation into cancer (EPIC-Norfolk).
Main outcome measures Concentrations of blood lipids.
Results Mean concentrations of total cholesterol and low density lipoprotein cholesterol decreased in a continuous relation with increasing daily frequency of eating in men and women. No consistent relation was observed for high density lipoprotein cholesterol, body mass index, waist to hip ratio, or blood pressure. Mean cholesterol concentrations differed by about 0.25 mmol/l between people eating more than six times a day and those eating once or twice daily; this difference was reduced to 0.15 mmol/l after adjustment for possible confounding variables, including age, obesity, cigarette smoking, physical activity, and intake of energy and nutrients (alcohol, fat, fatty acids, protein, and carbohydrate).
Conclusions Concentrations of total cholesterol and low density lipoprotein cholesterol are negatively and consistently associated with frequency of eating in a general population. The effects of eating frequency on lipid concentrations induced in short term trials in animals and human volunteers under controlled laboratory conditions can be observed in a free living general population. We need to consider not just what we eat but how often we eat.

Introduction

Small, time limited trials in humans and some case-control studies have indicated that people who eat frequently tend to have lower concentrations of total cholesterol and low density lipoprotein cholesterol than people who eat a gorging diet.[1–6] Results have been less conclusive with respect to concentrations of high density lipoprotein cholesterol, apolipoproteins, and serum glucose and secretion of insulin.[1 3 7]

Data from free living populations are limited, and it is not clear whether the effects observed in trials pertain only at the extremes of eating frequency or are continuous over the whole distribution of eating frequency. To investigate this we examined the relation between frequency of eating and concentrations of total cholesterol, low density lipoprotein cholesterol, and high density lipoprotein cholesterol in middle aged men and women in a British population based study.

Methods

We used data from the Norfolk cohort of the European prospective investigation into cancer.[8] This is an ongoing prospective cohort of approximately 25 000 people aged 45-75, resident in Norfolk, and recruited from general practice registers between 1993 and 1997. All participants gave informed consent. At the baseline survey participants completed a detailed health and lifestyle questionnaire and participated in a health examination.

Measurements—Trained nurses carried out a health check by following standardised protocols. We measured non-fasting serum concentrations of total cholesterol and high density lipoprotein cholesterol and calculated the concentration of low density lipoprotein cholesterol.[9]

Questionnaires—We assessed frequency of eating by using the question "How many times a day do you eat, including meals, snacks, biscuits with coffee breaks, etc?" We classified participants into five categories of eating frequency: one or two times a day, three times a day, four times a day, five times a day, and six or more times a day. Participants also completed a 160 item food frequency questionnaire.[10] We classified participants as current smokers or non-current smokers. We assessed physical activity by self reported evaluation of amount of activity involved in work: sedentary occupation, standing occupation, physical work (handling of heavy objects and use of tools), and heavy manual work.

Statistical analysis—We used data on participants aged 45-75 who had no missing information on eating

frequency, physical activity, lipid concentrations, nutrient intake, blood pressure, weight, height, or waist or hip circumference, which resulted in 14 666 participants (6890 men and 7776 women) being included in these analyses. We analysed the data, separately for men and women, by using the SAS software (SAS Institute, Cary, NC).

Results

Mean age did not differ linearly by eating frequency in men but was negatively related to eating frequency in women. Mean body mass index and waist to hip ratio decreased slightly and mean blood pressure increased with increasing reported eating frequency, but trends were not consistent. The percentage of current smokers and the mean alcohol intake were higher in people reporting eating two or fewer times a day. No clear trend for physical activity with eating frequency was observed in women, but men eating more frequently tended to be more likely to participate in physical or heavy manual work.

Mean concentrations of total cholesterol and low density lipoprotein cholesterol decreased with increasing eating frequency in both men and women in a continuous relation. Mean concentration was 0.29 mmol/l lower for total cholesterol and 0.26 mmol/l lower for low density lipoprotein cholesterol in men reporting eating once or twice a day compared with men eating six times or more a day; the differences for mean concentrations of total cholesterol and low density lipoprotein cholesterol in women were 0.22 mmol/l and 0.17 mmol/l. The concentration of high density lipoprotein cholesterol also decreased with increasing eating frequency in both men and women; the overall ratio of low density lipoprotein cholesterol to high density lipoprotein cholesterol decreased with increasing eating frequency.

Increased eating frequency was associated with higher daily intake of energy, as well as of fat, fatty acids, carbohydrate, and protein (see full version on *BMJ*'s website).

The table shows mean lipid concentrations and blood pressure in men and women after adjustment for age, body mass index, waist to hip ratio, smoking status, physical activity, total energy intake, and alcohol consumption. After adjustment for covariates the significant inverse relation of concentrations of total cholesterol and low density lipoprotein cholesterol to eating frequency was still present, but high density lipoprotein cholesterol concentration was no longer significantly inversely related to eating frequency in men.

Body mass index was weakly significantly associated with increasing eating frequency in men and women (after adjustment for all variables except body mass index) but in opposite directions: negatively in men and positively in women. Waist to hip ratio was still significantly negatively associated with eating frequency only in women (after adjustment for all variables except waist to hip ratio). Blood pressure was not significantly related to eating frequency in women but was positively associated in men.

Mean values for cardiovascular risk factors adjusted for age, obesity, cigarette smoking, physical activity, alcohol intake, and caloric intake with analysis of variance by reported daily eating frequency in men and women aged 45-75, EPIC-Norfolk 1993-7

	Eating frequency (No of times a day)					
	1 or 2	3	4	5	6 or more	P value*
Men	(n=353)	(n=2176)	(n=2525)	(n=1211)	(n=625)	
Cholesterol (mmol/l)	6.11	6.06	5.98	5.94	5.94	<0.01
LDL cholesterol (mmol/l)	4.06	3.98	3.91	3.86	3.86	<0.001
HDL cholesterol (mmol/l)	1.24	1.24	1.23	1.22	1.22	0.42
Body mass index (kg/m^2)*	26.2	26.5	26.4	26.1	26.1	0.02
Waist:hip ratio†	0.93	0.926	0.925	0.928	0.925	0.67
Systolic blood pressure (mm Hg)	136.0	136.1	135.3	135.8	137.7	0.01
Diastolic blood pressure (mm Hg)	84.3	84.0	83.4	83.8	85.2	<0.01
Women	(n=362)	(n=2182)	(n=2877)	(n=1511)	(n=844)	
Cholesterol (mmol/l)	6.26	6.25	6.19	6.12	6.08	<0.001
LDL cholesterol (mmol/l)	4.00	3.97	3.95	3.90	3.85	0.02
HDL cholesterol (mmol/l)	1.57	1.60	1.56	1.55	1.56	<0.01
Body mass index (kg/m^2)*	25.5	25.9	26.0	25.8	26.1	0.03
Waist:hip ratio†	0.793	0.787	0.784	0.784	0.784	0.03
Systolic blood pressure (mm Hg)	130.6	131.3	131.8	131.6	132.1	0.48
Diastolic blood pressure (mm Hg)	79.3	80.0	80.2	80.1	80.6	0.29

LDL=low density lipoprotein; HDL=high density lipoprotein.
*Adjusted for all variables except body mass index.
†Adjusted for all variables except waist:hip ratio.

Discussion

The fact that such an effect could be shown in this study is surprising, given the large potential errors in measurement. These include the single measurement of lipid concentrations to characterise individual participants as well as the assessment of eating frequency. Different participants might well interpret the question differently or report their usual eating frequency inaccurately; each person's eating pattern will also vary. Such random measurement errors are likely to obscure or minimise the effect size of any association.

Potential confounding factors

The inverse relation between blood lipid concentrations and eating frequency might be explained by confounding factors—that is, frequency of eating might simply be a marker of particular lifestyle factors, such as physical activity or alcohol intake, that may directly influence lipid concentrations. However, the relation persisted after adjustment for possible confounding variables including age, obesity, smoking, alcohol consumption, dietary intake, and physical activity. In contrast, blood pressure was not consistently inversely related to eating frequency. We cannot exclude residual confounding, but the specificity of the independent association of eating frequency with lipid concentrations but not with blood pressure makes it unlikely that higher eating frequency was simply a marker for a healthy lifestyle. The association was also consistent in men and women and in different age groups.

In addition, this finding is consistent with observational studies and controlled intervention studies on metabolic wards, which show a strong and independent relation between lipid concentrations and frequency of eating.[1–5 11] Our data show a decrease of approximately 5% in concentrations of total cholesterol and low density lipoprotein cholesterol in men and women who eat six or more times a day compared with those who eat once or twice a day. This finding was particularly striking in view of the increased energy intake, including fat intake, in people who reported eating more frequently.

Possible mechanisms

Several authors have proposed biological mechanisms that might underlie the lipid lowering effect of increased eating frequency. Gorging animals may have an adaptive metabolism—they are able to store energy from a few periodic loads of food, in contrast to nibbling animals, which feed continuously and have a steady metabolism.[12] This biological process, called "adaptive hyperlipogenesis," is characterised by higher gastrointestinal absorption of glucose and increased activity of pancreatic enzymes; increased ability to produce fat from glucose (that is, an enhanced hepatic lipogenesis possibly mediated by insulin action); increased hepatic synthesis of cholesterol; increased total mass of fat; and higher postprandial peaks of insulin and increased sensitivity to insulin in fat tissue.

Implications of the findings

These metabolic adaptations to gorging may also apply in humans, leading to an increased risk of cardiovascular disease due to changes in lipid profiles and glucose metabolism. Fábry reported 30%, 24%, and 20% prevalence of ischaemic heart disease in men aged 60-64 years reporting eating ≤3, 3-4, or ≥5 meals or snacks daily.[13]

The magnitude of effect in our study was a difference of approximately 0.25 mmol/l in cholesterol concentration (0.15 mmol/l after multivariate adjustment) between people eating six or more times daily and those eating once or twice daily. Although not large, this difference in cholesterol concentration is comparable to that achieved in metabolic studies involving alteration of intake of dietary fat or cholesterol,[14] as well as in the controlled trials of eating frequency.[1] This difference in cholesterol concentration is also associated in observational studies and trials with reductions in coronary heart disease ranging from 10% to 21%.[15,16] If applied population-wide, such reductions might have a substantial impact, particularly in older people, who have higher absolute rates of heart disease.

This study was conducted in an older cohort with relative high average cholesterol concentrations (around 6.1 mmol/l). Nevertheless, the people in the Norfolk cohort have cholesterol concentrations similar to or slightly lower than those reported for national British samples, which are about 6.4-6.8 mmol/l in this age group.[8,17]

Conclusion

Concentrations of total cholesterol and low density lipoprotein cholesterol are negatively and consistently associated with frequency of eating in a general population. We need to consider not just what we eat but how often we eat.

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Competing interests: None declared.

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What is already known on this topic

Studies in animals and small human trials indicate that eating frequency is inversely related to serum lipid concentrations

Few studies have examined this in a free living population under no dietary restrictions

What this study adds

In a free living population increased eating frequency was negatively and significantly associated with concentrations of total cholesterol and low density lipoprotein cholesterol

This association was still present after adjustment for body mass index, physical activity, cigarette smoking, and dietary intake

Mean age adjusted cholesterol concentrations differed by 0.25 mmol/l between people eating more than six times a day and those eating less than twice daily

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Endpiece

A chameleon

"Talking of a chameleon," he said: "Its master put it down on a tartan rug and it died of overexertion."

Jean Cocteau,
quoted by Liane de Pougy (1869-1950)