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Follicle Stimulating Hormone is Associated with Lipids in Postmenopausal Women

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Abstract

Postmenopause is associated with elevated levels of follicle stimulating hormone (FSH) compared to premenopause. There is evidence to suggest that high levels of FSH may influence lipid levels; however, the association between FSH and lipid levels in postmenopausal women has been largely unexplored.

Objective: The purpose of this study was to evaluate the relation between FSH and lipid levels in postmenopausal women from the Kuopio Ischaemic Heart Disease Risk Factor Study.

Methods: Postmenopausal women (n=588) aged 53–73 and not using hormone therapy were included. The relation between FSH and total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG) was evaluated using linear regression, adjusting for estradiol, body mass, smoking and other hormonal and lifestyle factors. The relation between FSH, dyslipidemia and abnormal lipid levels were also evaluated.

Results: FSH was positively and linearly associated with TC (p=0.001) and LDL-C (p=0.01) in all participants, with stronger relations seen in younger compared to older postmenopausal women. FSH was less strongly associated with HDL-C and TG. FSH was not associated with dyslipidemia; however, higher FSH was associated with increased risk of high TC (p=0.02) and high LDL-C (p=0.03).

Conclusions: These data suggest that higher FSH in postmenopausal women is related to higher levels of both TC and LDL-C.

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Keywords

Follicle stimulating hormone; Postmenopause; Lipids; Epidemiology

Introduction

Menopause is associated with adverse changes in cardiovascular disease (CVD) risk factors, including lipid levels. Although many of the physiological changes with menopause have been attributed to changes in estrogens, there is increasing evidence to suggest that follicle stimulating hormone (FSH) may have an independent effect on CVD risk[1,2]. FSH levels begin to rise during the perimenopausal years and remain elevated, with some variability, in postmenopause. The influence of the rise in FSH on CVD risk is controversial. Some studies have demonstrated that high FSH levels are associated with increased CVD risk[2,3], while others have shown that higher FSH levels are associated with lower risk[1,4,5]. Regardless of the direction of the association, there is emerging evidence that FSH may relate to CVD risk through its association with lipid levels[6,7].

Animal research has shown that FSH can act on low-density lipoprotein receptors (LDLR)[6], demonstrating a direct effect of FSH on lipids. Furthermore, data suggest that increasing FSH, independent of estrogen levels, increases both total cholesterol and LDL cholesterol[6]. While an association between lipids and FSH has been shown in some human studies[6,7], there is a scarcity of evidence in this area, especially regarding the relation in older postmenopausal women. Therefore, the aim of this study was to evaluate whether FSH levels are related to lipid levels in older postmenopausal women.

Methods

Study Population

Participants were members of the Kuopio Ischaemic Heart Disease Risk Factor Study (KIHD). This is a prospective cohort study in men and women in Eastern Finland designed to identify risk factors for metabolic and cardiovascular diseases. Female participants were enrolled in the KIHD study between March 1998 and February 2001. Eligible women were a random sample of 1,173 postmenopausal women living in Kuopio or the surrounding area. Women were recruited into four age groups: 53 to 56 years old, 59 to 62 years old, 64 to 68 years old, and 71 to 73 years old. Ultimately, 920 women (87.4% of those invited) completed the baseline clinical assessments and were enrolled in the cohort.

For the present analysis, women were excluded if they reported using hormone therapy (n=327) or if FSH (n=5) values were missing. The final sample size for this analysis was 588. The Research Ethics Committee at the University of Kuopio approved study procedures and participants provided written informed consent before beginning any study procedures.

Blood Collection and Biochemical Measurements

Blood samples were collected from participants at a clinic visit between 8 and 10 AM, while the participant was fasted and had abstained from smoking cigarettes for 12 hours, and

alcohol consumption for 3 days. Plasma and serum was separated and then stored, within 1 hour of venipuncture, at −20°C or −80°C until analysis. Biochemical measures, including hormonal factors such as FSH, 17-beta estradiol, sex-hormone binding globulin (SHBG), and testosterone were assessed between June 2001 and February 2002.

FSH, 17-beta estradiol, and testosterone were measured using commercially available immunoradiometric assays. Serum FSH was determined with sandwich technique, applying an immunoradiometric assay manufactured by Diagnostic Product Corporation (Coat-A-Count FSH IRMA, Siemens, Erlangen, Germany). Serum 17-beta-estradiol (E2) was assayed between 1999 and 2001 with a radioimmunoassay manufactured by DiaSorin (Stillwater, Minnesota). Serum testosterone (17b-hydroxy-4-androsten-3-one) was determined with a Spectria Testosterone (125I) radioimmunoassay kit (Orion Diagnostica, Espoo, Finland). 125I label measurements for FSH, E2, and testosterone were carried out by gamma counter Wallac 1261 MultiGamma using a RiaCalc LM Evaluation Program. Coefficients of variation were 5%, 7.6–12%, and 7.9–12.2%, respectively[5]. SHBG was measured with a fluoroimmunoassay (AutoDELFIA SHBG, Wallac Co., Turku, Finland), with coefficients of variation of 6.0–9.0%[8]. Total cholesterol (TC), LDL cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were assessed enzymatically (CHOD-PAP method, Boehringer Mannheim, Mannheim, Germany). Coefficients of variation were 2.3%, 5.2%, 9.2% and 1.9%, respectively[9,10].

Clinical Measures and Questionnaire Assessments

Clinical and reproductive outcomes such as time since the final menstrual period, oral contraceptive use, history of hormone therapy use, hysterectomy and oophorectomy were evaluated based on self-report. Similarly, participants were asked about behavioral factors such as smoking and physical activity with validated questionnaires[11]. A trained interviewer then reviewed all questionnaire responses. History of cardiovascular and metabolic diseases, along with medication use, was assessed during physician-administered interviews.

Resting blood pressure was measured 6 times during the clinic visit, and mean blood pressure was calculated by averaging three supine, one standing, and two seated measurements, with 5 minutes rest in between measures. Height, weight, waist and hip circumference were measured. Height and weight were used to calculate body mass index (BMI) as weight (kg) divided by height (m^2). Waist-to-hip ratio (WHR) was calculated from circumference measurements.

Statistical Analyses

All statistical analyses were completed in SPSS v24. Statistical significance was accepted at an alpha level of 0.05. Participants were initially divided into quartiles based on FSH levels. Baseline characteristics were compared across quartiles using ANOVAs or chi-square tests.

Linear regression was used to evaluate the relations between FSH and lipid levels. Lipid variables were log transformed to improve normality and included TC, LDL-C, HDL-C, and TG. Model 1 adjusted *a priori* for age, date of examination, estradiol, SHBG and testosterone levels, age of menarche, last menstruation age, oral contraceptive use, hormone therapy use, and history of hysterectomy or oophorectomy. Model 2 included all covariates

in model 1 as well as waist-to-hip ratio, BMI, systolic and diastolic blood pressure, physical activity levels and smoking status. The fully adjusted model included covariates in model 2 and use of lipid-lowering medications. Twenty seven participants reported taking lipid lowering medications. All of those participants did not meet the criteria for having dyslipidemia, as outlined below. Model 2 was also run in participants not taking lipid lowering medications. The median FSH value for each quartile was modeled as a continuous variable to assess linear trends. To evaluate if relations of FSH and lipids varied by age and BMI, we conducted analyses stratified by these factors and tested for effect modification with multiplicative interaction terms.

We then used logistic regression to evaluate whether FSH levels were associated with dyslipidemia, as well as high TC (≥6.20 mmol/L, ≥240 mg/dL), high LDL-C (≥4.1 mmol/L, ≥160 mg/dL), low HDL-C (<1.0 mmol/L,<40mg/dL) and high TG (≥2.30 mmol/L, ≥200 mg/dL)[12]. Dyslipidemia was defined as meeting any of the criteria for abnormal lipid levels, as defined above, or the use of lipid-lowering medications. All abnormal lipid outcomes also included use of lipid lowering medications. Covariates were selected based on which variables led to the greatest change in the odds ratio for FSH. FSH was included as a continuous variable. Covariates meeting selection criteria included BMI, waist-to-hip ratio, SHBG, estradiol, date of examination, and age.

Results

When comparing participant characteristics based on FSH quartiles, there were significant, though modest, differences across groups (Table 1). BMI, WHR, estradiol, and SHBG were lower at higher FSH quartiles. Physical activity was higher at higher FSH quartiles. Despite these differences, many variables were similar across groups including age at menopause, past hormone therapy use, smoking status, and parity.

In unadjusted models, LDL-C (P=0.15) and TC (P=0.01) levels increased across FSH quartiles (Table 2). We observed a significant positive linear relation between FSH and TC (model 3, P for trend 0.001), and LDL-C (model 3, P for trend 0.007). Results from minimally and fully adjusted models for these lipids were virtually identical. HDL-C levels were higher among women in quartiles 2–4 for FSH than quartile 1 in model 1 (P for trend = 0.02), with results somewhat attenuated in our fully adjusted model (P = 0.06). FSH was not consistently associated with TG levels. Results from a sensitivity analysis excluding participants taking lipid-lowering medications (n=27) were very similar to the main analysis (data not shown).

We assessed the FSH–lipid relations in fully adjusted models stratified by age (younger: 53–62 years old; older: 64–73 years old). We did not observe evidence of significant effect modification by age ($P_{interaction}$ all >0.05), but results varied somewhat between older and younger women. Though our power for analyses was lower and standard errors were wider than in the main analysis, results for FSH and LDL-C were stronger in magnitude in younger women, while associations for HDL-C were more pronounced in older women (Table 3). We found no evidence of effect modification based on BMI ($P_{interaction}$ all >0.05; data not shown).

Finally, we assessed the association of continuous FSH levels with risk of dyslipidemia and abnormal levels of each lipid, as defined above (Table 4). FSH levels were not associated with prevalent dyslipidemia; the percentage of participants with dyslipidemia in FSH quartiles 1–4 was 52.4%, 49.7%, 45.5%, and 51.0%, respectively and did not differ across quartiles (p=0.71). FSH was significantly associated with higher risk of elevated TC and LDL-C. Each 10-unit increase in FSH was associated with a 13% higher risk of elevated TC (95% CI = 2%−24%) and a 12% higher risk of elevated LDL-C (95% CI = 1%−23%). Results suggested that higher FSH was associated with somewhat lower risk of abnormal HDL-C and TG, but were not significant. We found no evidence of effect modification based on body mass index or age ($P_{interaction}$ all >0.05; data not shown).

Discussion

Findings from this population-based study suggest that FSH is associated with higher levels of TC and LDL-C and increased risk of abnormal TC (≥6.20 mmol/L) and LDL-C (≥4.1 mmol/L) in postmenopausal women. The results also provide evidence that higher FSH is associated with better HDL-C (>1.0 mmol/L) and triglyceride levels (<2.30 mmol/L), although these associations did not reach statistical significance. Importantly, relations persisted after adjustment for estradiol and other hormones, CVD risk factors, and lipid lowering medication use. Finally, our data indicate that these relations may vary somewhat by age, though our power to detect significant differences was low due to the small sample sizes of individual strata.

Data from the animal literature addresses the biological mechanisms by which FSH may directly influence lipid levels. In ovariectomized mice, when FSH was elevated independent of estradiol, there was an increase in both TC and LDL-C. This increase was associated with reduced LDLR expression. FSH receptors are also present in human liver tissue, and when exposed to FSH, there is reduced expression of LDLR[6]. FSH has also been shown to stimulate lipid biosynthesis in chicken adipose tissue[13] and lipid droplet formation in human adipose tissue[14], again demonstrating that FSH may have direct effects on lipid metabolism and specifically on TC and LDL-C.

Few human studies have evaluated the effect of FSH on lipids, and results have been inconsistent. An analysis comparing Chinese postmenopausal women with high vs. low levels of FSH found that higher FSH was associated with higher levels of LDL-C and TC[6]. Further, a 30% reduction in FSH due to hormone therapy, equivalent to ~25IU/L change, was associated with a reduction in LDL-C of 0.14 mmol/L and a reduction in TC of 0.19 mmol/L. However, a second study of postmenopausal Chinese women reported a direct association between FSH and HDL-C and an inverse relation with TG and LDL-C[1].

Explanations for differences in findings between studies regarding LDL-C are unclear, but may be influenced to some extent by age. While our power for stratified analyses was low, data suggested that positive associations of FSH with LDL-C were stronger in younger postmenopausal women (ages 53–62) than in older postmenopausal women (ages 64–73). In contrast, positive associations with HDL-C were stronger in older women. A changing relation between FSH and CVD risk factors with age is supported by the literature. Wide et

al., reported differences in FSH isoforms in postmenopausal compared to premenopausal women, potentially leading to a higher FSH half-life in postmenopausal women and therefore influencing its biological effects[15]. Evaluating potential differences in function of FSH with age is an important area for future research.

While this study provides insight into the relation between lipid levels and FSH in postmenopausal women, it has some limitations. Study participants were postmenopausal women in Finland, therefor results may not be generalizable to other populations with greater racial and ethnic diversity; however, the physiologic relation of FSH and lipid levels is unlikely to vary by these characteristics. Further, this is a cross-sectional analysis, therefore we were unable to evaluate the temporality of the relation between FSH and lipid levels.

We used immunoassay to measure sex steroid hormone levels in our population rather than direct methods such as mass spectrometry, as is more commonly used in clinical practice. However, studies comparing steroid hormone levels assessed by the techniques indicate that immunoassay provides valid results, and is sensitive enough to accurately rank participants, as is the objective in many epidemiologic studies

Misclassification of participants by relative sex steroid levels is thus likely to be minimal. However, we suggest that future studies evaluating the clinical utility of FSH measures should consider using mass spectrometry.

Finally, future investigation of other lipid related variables will be important in this population. For example, there may be effects of FSH on other lipoprotein metrics, including apolipoprotein B or on proteins such as proprotein convertase subtilsin kexin type 9 (PCKS9), which modify LDLR recycling.

Conclusion

Overall, this study indicates that FSH may be associated with lipid levels in postmenopausal women, and that relations vary between lipids and potentially by age. Further evaluation of these relations and the physiologic mechanisms underlying them is warranted, especially via prospective studies that can provide a clearer understanding as to whether FSH is related to postmenopausal CVD risk.

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Table 1.

Participant Characteristics by Quartile of Follicle Stimulating Hormone, Kuopio Ischaemic Heart Disease Risk Factor Study (1998–2001)

FSH Quartile (n)	**Quartile 1 (n=147)**	**Quartile 2 (n=149)**	**Quartile 3 (n=145)**	**Quartile 4 (n=147)**	
FSH range (IU/l)	**1–39.3**	**39.4–50.0**	**50.1–61.8**	**61.9 to 136.8**	
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	P
Age (yrs)	64.5 (6.9)	65.1 (5.9)	64.4 (6.1)	62.8 (6.9)	0.02
BMI (kg/m^2)	31.1 (5.7)	29.0 (5.4)	28.7 (5.0)	26.8 (4.4)	<0.001
WHR	0.87 (0.07)	0.85 (0.06)	0.84 (0.06)	0.83 (0.06)	<0.001
Estradiol (pmol/ml)	55.8 (77.6)	35.1 (19.8)	32.5 (12.5)	34.1 (19.5)	<0.001
Testosterone (nmol/l)	1.5 (2.9)	1.1 (0.5)	1.1 (0.5)	1.1 (0.5)	0.062
SHBG (nmol/L)	45.6 (23.2)	49.5 (21.2)	55.0 (24.3)	58.4 (28.0)	<0.001
SBP (mmHg)	140.8 (20.4)	141.1 (17.3)	136.2 (16.4)	135.8 (16.4)	0.01
DBP (mmHg)	80.9 (9.7)	80.5 (8.7)	79.6 (8.3)	80.4 (8.5)	0.66
Physical Activity (MET-hr/day)	45.2 (5.9)	46.1 (7.1)	46.3 (6.1)	47.4 (7.5)	0.05
Parity	2.8 (1.4)	2.7 (1.6)	2.8 (1.7)	2.3 (1.3)	0.08
	n (%)	n (%)	n (%)	n (%)	P
Age at menopause (yrs)	49.7 (4.4)	49.4 (4.3)	48.9 (4.8)	49.2 (4.3)	0.50
Current Smoker	12 (8%)	14 (9%)	16 (11%)	7 (5%)	0.25
Past Smoker	19 (13%)	15 (10%)	11 (8%)	19 (13%)	0.37
Past HT use	38 (26%)	45 (30%)	48 (33%)	49 (33%)	0.58

SD: standard deviation, FSH: follicle stimulating hormone, BMI: body mass index, SHBG: sex hormone binding globulin, SBP: systolic blood pressure, DBP: diastolic blood pressure: HDL-C: high-density lipoprotein cholesterol, LDL-C: low-density lipoprotein cholesterol, HT: hormone therapy

Table 2.

Follicle Stimulating Hormone and Mean Lipid Levels in Postmenopausal Women, Kuopio Ischaemic Heart Disease Risk Factor Study (1998–2001).

	Unadjusted[a]	Model 1[b]			Model 2[c]			Model 3[d]		
	Mean (SD)	Beta	SE	P	Beta	SE	P	Beta	SE	P
Total Cholesterol										
FSH Q1	5.6 (0.7)		Ref			Ref			Ref	
FSH Q2	5.8 (0.9)	0.014	0.008	0.09	0.014	0.008	0.10	0.014	0.008	0.08
FSH Q3	5.8 (0.9)	0.016	0.008	0.05	0.015	0.008	0.04	0.018	0.008	0.04
FSH Q4	5.9 (1.0)	0.025	0.008	0.004	0.025	0.009	0.003	0.025	0.009	0.004
p for trend	0.01			0.002			0.001			0.001
LDL-C										
FSH Q1	3.6 (0.7)		Ref			Ref			Ref	
FSH Q2	3.8 (1.0)	0.013	0.013	0.29	0.014	0.013	0.26	0.015	0.013	0.23
FSH Q3	3.8 (0.9)	0.022	0.013	0.09	0.025	0.013	0.05	0.026	0.013	0.05
FSH Q4	3.9 (1.0)	0.031	0.013	0.02	0.035	0.013	0.01	0.035	0.013	0.01
p for trend	0.15			0.01			0.01			0.007
HDL-C										
FSH Q1	1.3 (0.3)		Ref			Ref			Ref	
FSH Q2	1.3 (0.3)	0.021	0.011	0.06	0.018	0.011	0.12	0.018	0.011	0.12
FSH Q3	1.4 (0.3)	0.021	0.012	0.07	0.019	0.012	0.11	0.019	0.012	0.11
FSH Q4	1.4 (0.3)	0.025	0.012	0.04	0.018	0.012	0.13	0.018	0.012	0.13
p for trend	<0.001			0.02			0.06			0.06
Triglycerides										
FSH Q1	1.4 (0.7)		Ref			Ref			Ref	
FSH Q2	1.3 (0.8)	0.015	0.021	0.47	0.025	0.02	0.23	0.021	0.020	0.29
FSH Q3	1.2 (0.5)	0.010	0.022	0.66	0.021	0.021	0.49	0.014	0.021	0.50
FSH Q4	1.2 (0.6)	0.014	0.022	0.51	0.021	0.022	0.09	0.037	0.021	0.08
p for trend	0.01			0.67			0.21			0.17

FSH: follicle stimulating hormone, Q: quartile, SE: standard error;

[a]Unadjusted, untransformed mean total cholesterol (mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), high-density lipoprotein-cholesterol (HDL-C, mmol/L), and triglycerides (mmol/l). P-value from ANOVA

[b]Lipid levels log transformed to improve normality in all regression models. Model 1 adjusted for age (continuous), year of study entry (continuous), estradiol (quartiles), testosterone (quartiles), sex-hormone binding globulin (quartiles), age at menarche (above and below median), last menstruation age (above and below median), duration of oral contraceptive use (above and below median), duration of hormone therapy use (above and below median), history of hysterectomy (yes, no), history of oophorectomy (yes, no).

[c]Model 2 adjusted for model 1 covariates and systolic blood pressure (continuous), diastolic blood pressure (continuous), smoking status (never, past, current + pack-years above median; current + pack-years below median), physical activity (quartiles), body mass index (continuous), and waist-to-hip ratio (continuous).

[d]Model 3 adjusted for model 2 covariates and use of lipid lowering medication (yes, no)

Table 3:

Follicle Stimulating Hormone and Mean Lipid Levels in Postmenopausal Women, Stratified by Age, Kuopio Ischaemic Heart Disease Risk Factor Study (1998–2001).

	Ages 53 to 62 years (n = 244)				Ages 64–73 years (n = 344)			
	Mean (SD) [a]	Beta [b]	SE	P	Mean (SD) [a]	Beta [b]	SE	P
Total Cholesterol								
FSH Q1	5.6 (0.7)		Ref		5.5 (0.8)		Ref	
FSH Q2	5.8 (1.0)	0.023	0.013	0.11	5.7 (1.0)	0.005	0.011	0.64
FSH Q3	5.8 (0.9)	0.026	0.013	0.06	5.7 (0.8)	0.008	0.011	0.49
FSH Q4	5.9 (1.0)	0.021	0.013	0.10	6.0 (1.0)	0.024	0.012	0.06
p for trend				0.22				0.05
LDL-C								
FSH Q1	3.6 (0.7)		Ref		3.6 (0.7)		Ref	
FSH Q2	3.8 (1.0)	0.022	0.022	0.33	3.8 (1.0)	0.002	0.016	0.89
FSH Q3	3.8 (0.9)	0.048	0.021	0.03	3.7 (0.8)	0.003	0.017	0.84
FSH Q4	3.9 (1.0)	0.041	0.021	0.05	3.9 (1.0)	0.026	0.019	0.16
p for trend				0.14				0.01
HDL-C								
FSH Q1	1.3 (0.3)		Ref		1.2 (0.3)		Ref	
FSH Q2	1.3 (0.3)	0.027	0.018	0.13	1.3 (0.3)	0.011	0.016	0.48
FSH Q3	1.4 (0.3)	0.014	0.017	0.42	1.4 (0.3)	0.024	0.017	0.15
FSH Q4	1.4 (0.3)	0.008	0.017	0.57	1.4 (0.4)	0.022	0.018	0.23
p for trend				0.42				0.09
Triglycerides								
FSH Q1	1.4 (0.7)		Ref		1.4 (0.7)		Ref	
FSH Q2	1.4 (0.8)	-0.018	0.035	0.61	1.4 (0.6)	0.032	0.026	0.23
FSH Q3	1.2 (0.6)	-0.001	0.033	0.98	1.2 (0.6)	0.021	0.028	0.46
FSH Q4	1.2 (0.6)	0.044	0.032	0.17	1.2 (0.6)	0.030	0.030	0.32
p for trend				0.54				0.28

FSH: follicle stimulating hormone, Q: quartile, SE: standard error;

[a] Unadjusted, untransformed mean total cholesterol (mmol/L), low-density lipoprotein cholesterol (LDL-C, mmol/L), high-density lipoprotein-cholesterol (HDL-C, mmol/L), and triglycerides (mmol/l).

[b] Lipid levels log transformed to improve normality in all regression models. Model adjusted for age (continuous), year of study entry (continuous), estradiol (quartiles), testosterone (quartiles), sex-hormone binding globulin (quartiles), age at menarche (above and below median), last menstruation age (above and below median), duration of oral contraceptive use (above and below median), duration of hormone therapy use (above and below median), history of hysterectomy (yes, no), history of oophorectomy (yes, no).

systolic blood pressure (continuous), diastolic blood pressure (continuous), smoking status (never, past, current + pack-years above median; current + pack-years below median), physical activity (quartiles), body mass index (continuous), waist-to-hip ratio (continuous), and use of lipid lowering medication (yes, no)

Table 4.

Association of Follicle Stimulating Hormone and Abnormal Lipid Level in Postmenopausal Women, Kuopio Ischaemic Heart Disease Risk Factor Study (1998–2001).

	n	beta per 1 IU higher FSH[c]	SE	OR per 10 IU higher FSH	95% Confidence Interval	P
Dyslipidemia (all lipids) [a,b]						
No	296	reference				
Yes	292	0.003	0.005	1.03	0.94–1.13	0.57
Total Cholesterol[b]						
≤ 6.2 mmol/L[a]	399	reference				
> 6.2 mmol/L	189	0.012	0.005	1.13	1.02–1.24	0.02
LDL-C[b]						
< 4.1 mmol/L[a]	374	reference				
≥ 4.1 mmol/L	214	0.011	0.005	1.12	1.01–1.23	0.03
HDL-C[b]						
≥ 1.0 mmol/L[a]	491	reference				
< 1.0 mmol/L	97	-0.010	0.007	0.90	0.78–1.04	0.15
Triglycerides[b]						
< 2.3 mmol/L[a]	520	reference				
≥ 2.3 mmol/L	68	-0.012	0.008	0.89	0.75–1.05	0.17

OR: odds ratio; SE: standard error

[a] Lipid classifications based on ATP III guidelines[9].

[b] Case status also includes use of lipid-lowering medication

[c] Adjusted for age (continuous), date of study entry, sex hormone binding globulin (continuous), estradiol (continuous), body mass index (continuous), and waist to hip ratio (continuous).