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Increased usual physical activity is associated with a blunting of the triglyceride response to a high-fat meal

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Abstract

Background: Post-prandial lipemia (PPL), defined as a prolonged or elevated rise in triglycerides that accompanies fat feeding, is a significant risk factor for coronary heart disease (CHD) and associated comorbidities. The impact of PPL on CHD risk is underscored by the preponderance of each day spent in the post-prandial state.

Objective: In this study, we evaluated cross-sectionally the association between usual (i.e., non-interventional) physical activity and the 6-hour triglyceride response to a standardized high-fat meal.

Methods: The high-fat meal intervention was carried out in 671 apparently healthy individuals as part of the Hereditary and Phenotype Intervention (HAPI) Heart Study. Triglyceride levels were measured in the fasting state and during six hours following administration of a standardized fat challenge. We defined PPL response as the triglyceride area under the fat load curve (AUC) and measured physical activity using accelerometers that were worn continuously over a 7-day period.

Results: Physical activity levels decreased with increasing age and were higher in men than women (both $p < 0.001$). The triglyceride AUC increased with increasing age in both men and women (both $p < 0.001$) and was also higher in men than in women (age-adjusted $p = 9.2 \times 10^{-12}$). Higher physical activity levels were associated with a lower triglyceride AUC ($p = 0.003$), adjusting for age, sex, BMI, and fasting low-density lipoprotein (LDL).

Conclusion: These results suggest that the protective benefits of physical activity on cardiovascular health may operate, at least in part, through reduction of the PPL triglyceride response.

Keywords

Post-prandial lipemia; physical activity; non-fasting triglycerides; cardiovascular risk; accelerometer; Amish; oral fat tolerance test; high-fat meal

Introduction

Historically, the association of lipid levels with cardiovascular disease (CVD) risk has been based on fasting cholesterol levels and the robustness of the lipid-CVD associations is due largely to the fact that circulating levels of total, high- and low-density lipoproteins change relatively little during the course of the day. In contrast, triglyceride (TG) levels fluctuate considerably with feeding, depending on the amount and content of the meal, as well as other factors that influence the absorption and clearance of TG particles. The importance of elevated TG levels following a meal, or post-prandial lipemia (PPL), to CVD risk has been recognized for nearly 40 years (1–3).

The strongest evidence in support of PPL as a CVD risk factor is derived from multiple large population studies that have consistently demonstrated nonfasting TG levels to be independently associated with incident CVD, and even more strongly associated than fasting TG levels (4, 5). For example, in the Women's Health Study, subjects in the highest tertile of the nonfasting TG distribution experienced a 2.5-fold higher incidence of CVD compared to subjects in the lowest tertile of the distribution (5). Similarly, women in the Copenhagen City Heart Study with nonfasting TGs between 1–1.99 mmol/L had a 1.9-fold higher incidence of ischemic heart disease compared to women with TGs < 1 mmol/L; women with nonfasting TGs ≥ 5 mmol/L had a 3.8-fold higher incidence.

The atherogenic consequence of PPL has been attributed to delayed clearance of TG- rich lipoproteins and enhanced hepatic secretion of TG-rich very low density lipoprotein particles that contribute to postprandial inflammation (6, 7) and endothelial dysfunction (8). The contribution of PPL to CVD risk is particularly significant in Westernized societies where a sizeable portion of each day is spent digesting and absorbing excessive amounts of dietary fat (9).

Based on the observations summarized above, it is widely believed that reduction of PPL may reduce the risk of CVD. It is now well established that short bouts of aerobic exercise can reduce postprandial TG concentrations, although the effects of exercise interventions are transient, varying according to the duration and intensity of the exercise (see Peddie et al. (10)). However, it is not clear how results from these regimented exercise intervention studies apply to individuals in the general population where there may be wide ranges in 'usual' physical activity levels, and specifically, whether physically active individuals in general exhibit a lower PPL response than less active or sedentary individuals. To address this issue, we performed a secondary analysis of data collected from the Heredity and Phenotype Intervention (HAPI) Heart Study (11), in which a standard oral fat tolerance test had been administered to measure the dynamic changes in TG response to a large cohort of healthy men and women for whom detailed measures of physical activity levels were available over a 7-day period. With these data we tested the hypothesis that higher levels of daily noninstructional physical activity are associated with a lower PPL response.

Methods

The HAPI Heart Study, a study designed to evaluate the genetic response to four short-term interventions affecting cardiovascular risk factors. This study included a total of 868 apparently healthy Amish individuals aged 20 years and older from the Lancaster County, PA, Old Order Amish community who were recruited into the study between 2003 and 2006. Recruitment procedures, including response rates and exclusion criteria, have been previously described (11). Of the 868 HAPI Heart Study participants, 838 (97%) participated in the high-fat challenge intervention, the goal of which was to evaluate determinants of the TG response following ingestion of a standardized high-fat meal.

Following an overnight fast, study participants underwent a physical examination and medical history assessment at the Amish Research Clinic Study in Lancaster, PA. Blood samples were collected for measurement of lipids and lipoproteins and selected biochemical parameters. An oral fat tolerance test (OFTT) was also performed at this visit in which the high-fat meal was prepared as a whipping cream milk shake, standardized to body size and consisting of 782 calories per m² of body surface, with 77.6%, 19.2%, and 3.1% of calories derived from fat, carbohydrates, and protein, respectively. In addition to baseline, triglyceride levels were measured at 1, 2, 3, 4, and 6 hours following ingestion of the meal. During the 6-hour follow-up period, participants were sedentary and remained fasting, except for water.

Beginning on the day following the high-fat challenge, we provided a subset of 671 study participants with Actical activity monitors (versions 8.2 and 8.3; Mini Mitter Co, Inc, Bend, Oregon) to obtain detailed measures of physical activity. Accelerometry is a well-established method to quantify physical activity (12). Actical monitors contain piezo-electric sensors that generate an electronic charge based on activity that can be converted to activity counts. Participants wore the monitors on the hip for 24 hours continuously over a 7-day period, during which time activity counts were collected every 15 seconds. We recorded the number of activity counts over the entire 7-day period, and for purposes of this analysis, this 7-day measure can be considered a measure of physical activity levels. Methodological details regarding the physical activity measurements have been previously described (13). All study procedures were approved by the University of Maryland Institutional Review Board.

We characterized the TG response to the high-fat meal as the area under the fat tolerance test curve, using the trapezoid method to measure the area under the curve (AUC) based on the TG levels measured at 1, 2, 3, 4, and 6 hours post-fat challenge. Prior to analysis we normalized the distribution of physical activity counts, TG AUC, total cholesterol, BMI, and fasting TG using a natural log-transformation, and analyses were performed on the transformed variables. Linear models were used to evaluate the associations of TG response and physical activity with age and sex. We then tested the association of TG response with physical activity by regressing physical activity against TG response in men and women separately, while adjusting for age as a covariate. We additionally tested whether the association of physical activity with TG response differed between men and women by combining men and women together in the analysis and testing for a sex*physical activity interaction. To account for the relatedness between study individuals, we employed a mixed

model that included the family relationship matrix as a random effect as implemented in the Mixed Model for Pedigree Analysis (MMA) software (14).

Results

Accelerometry was collected in 671 of the 838 subjects (out of 868 total HAPI Heart Study participants) who underwent the high-fat challenge. There were no significant differences in age, sex, or BMI between subjects for whom accelerometry was collected vs not collected (data not shown). Characteristics of these subjects are provided in Table 1. Compared to men, women were slightly older (mean 45.2 vs 42.0 yrs; $p = 0.007$), had higher BMI (mean 27.7 vs 25.6 kg/m²; $p < 0.001$), fasting TG (median 60.0 vs 53.0 mg/dl; $p = 0.04$), total cholesterol (mean 215.0 vs 202.9 mg/dl $p = 0.003$), and lower levels of physical activity (median counts 331,828 vs 467,152; $p < 0.001$) and TG AUC (median 678.0 vs 776.0; $p < 0.001$).

As expected, physical activity levels decreased with age, with this trend apparent in both men and women ($p < 0.001$ for both, Figure 1). With increasing age, there was an increase in PPL response to the high-fat challenge, a trend again observed in both men and women ($p < 0.001$ for both) (Figure 2). Following adjustment for age and sex, physical activity levels were positively correlated with levels of total and LDL cholesterol and inversely correlated with fasting TG levels (all $p < 0.01$). Physical activity levels were not significantly correlated with BMI ($p = 0.62$).

Using a mixed model approach to adjust for age, sex, and kinship, we evaluated the associations of selected variables with TG AUC. These analyses confirmed that higher TG AUC was significantly associated with older age (adjusted for sex and kinship only), and that higher TG AUC was significantly associated with higher BMI, higher total and LDL cholesterol, and higher baseline TG (all $p < 0.001$) (Table 2). Higher physical activity levels were also significantly associated with lower TG AUC ($p = 0.017$) (Table 2). Fasting levels of HDL cholesterol and TG were highly correlated ($r = -0.495$), as were HDL AUC and TG AUC ($r = -0.567$).

Through multivariable association testing, we further confirmed that higher physical activity levels remained associated with lower TG AUC even after adjustment for BMI ($p = 0.019$), and with the joint inclusion of BMI and fasting LDL as covariates ($p = 0.003$) (Table 3). When expressed as quartiles of physical activity, subjects in the lowest compared to highest quartile of physical activity experienced a 17% (95% confidence interval 5%–29%) increase in TG AUC, after adjusting for age, sex, BMI, and fasting LDL (Figure 3). For a person at a gender-specific mean age of this cohort and with mean LDL-C and BMI, the predicted PPL TG AUC are 853.8, 819.6, and 791.0 for a man (at mean age 42.0 years), and 755.0, 728.1, 698.6 for a woman (at mean age 42.2 years) for physical activity levels at the 25%, 50% and 75% percentile, respectively.

Finally, we considered whether the association of physical activity and PPL response differed by age or sex, by including age*physical activity and sex*physical activity

interaction terms in the regression model. In neither case did we detect strong evidence for interaction (both $p > 0.05$).

We have previously identified a null mutation (R19X; rs76353203) in *APOC3* that is associated with a blunted response to TG AUC (15). This variant, which is highly enriched in the Lancaster Amish (minor allele frequency = 0.028), prematurely truncates the APOC-III protein, rendering it nonfunctional. Because APOC-III impairs catabolism and hepatic uptake of apoB-containing lipoproteins (including TGs), disruption of *APOC3* leads to reduced levels of TGs in the circulation. To rule out potentially confounding effects of the TG-lowering effects of this variant on our results, we repeated our analyses of the physical activity-PPL association after excluding 34 subjects heterozygous for the R19X mutation. Results were essentially unchanged (e.g., $p = 0.03$ for age- and sex-adjusted model; $p = 0.005$ for age, sex, BMI, and LDL-adjusted model).

Discussion

In this investigation, we observed that higher daily physical activity is significantly associated with a decrease in PPL response in a large cohort of apparently healthy subjects recruited from the community. This association occurs independently of BMI and is present in both men and women. To our knowledge, the current study is among the first to investigate systematically the effect of daily non-instructional physical activity on the PPL response in contrast to prior studies (see below) that evaluated the PPL response following instructional exercise physical activity. As such, this is a clinically relevant observation because the majority of each day is spent in the non-fasting state and the ensuing elevated PPL is associated with enhanced atherogenicity. Consequently, reducing the magnitude of TG excursions following a meal and/or reducing the time spent in the PPL state may be an important strategy for reducing CVD risk.

It has been well documented that acute bouts of exercise can attenuate the rise in TG levels following a high-fat meal, although the effects are short-lived (10). Studies of a variety of short-term exercise regimens of varying times and intensities have reported reductions in post-prandial TG ranging from 10–27% (reviewed by Miyashita (16)). While there remains some uncertainty about the intensity and duration of the physical activity required to attenuate the post-meal lipemic response (16, 17), available data suggests that the window during which acute exercise can attenuate PPL ranges between 18 hours prior to the high-fat meal to 90 minutes following the high-fat meal (18–20). More generally, the available data suggest that high bouts of chronic exercise alone, without an accompanying recent bout of exercise, do not markedly affect the post-meal lipemic response, and this has been reported even among highly active individuals (20, 21). It is thus possible that the association of 7-day physical activity with PPL reduction observed in the Amish may be attributable to higher physical activity levels on the day preceding the high-fat meal. Unfortunately, we are unable to disentangle the independent effects of long-term physical activity from activity levels on the day prior to the high-fat meal testing because our 7-day assessment of physical activity levels began on the day following the OFTT due to the original design of the HAPI Heart Study.

Overall, these results may have important public health implications because they suggest that regular physical activity, as opposed to study-driven physical exercise interventions, is associated with reduced PPL. As elevated PPL response has been associated with increased incidence of CAD (4, 5), further studies are needed to determine whether reducing PPL corresponds to CVD risk reduction.

Our study has multiple strengths. First, we studied a large population-based cohort and evaluated the impact of ‘usual’ levels of physical activity on the PPL response in a ‘free-living’ setting. Second, we measured PPL using a carefully standardized OFTT protocol administered to 671 subjects who were recruited from the community. The standardized meal helps eliminate variations in PPL response solely due to meal composition immediately prior to the PPL measures. Third, we obtained a robust assessment of daily physical activity levels using accelerometry collected over a 7-day period. In contrast, many other studies have assessed physical activity levels by self-report. Our study was not designed to evaluate the differential contribution of physical activity intensity or duration. Finally, the Amish population is very homogeneous with respect to their rural lifestyle, education levels, and other socioeconomic factors. Collectively, these features help minimize other potentially confounding variables that hinder many observational studies.

Our investigation also has some limitations. First, the Amish community is characterized by relatively high levels of physical activity compared to non-Amish (22–26), and it is conceivable that the benefits of high physical activity observed in this community may not be generalizable to more sedentary or less physically active populations. This issue is worthy of further investigation. Second, although we measured the PPL TG response to a standardized high-fat meal, this meal had a very high fat content and omits many other nutrients so that it does not reflect the nutrient composition of typical meals. Multiple dietary factors influence the absorption and metabolism of dietary lipid, including total fat, fatty acid composition, fiber, carbohydrate, protein, alcohol consumption and overall energy balance, and these will also have an impact on circulating TG levels. While the magnitude of association we observed between PPL response and physical activity in this study may differ from that observed in response to a mixed whole diet, the direction of protective modifying effect of regular physical activity on PPL TG is expected to be preserved. Finally, this study was carried out in an Amish isolate population characterized by a unique and homogenous lifestyle. The Lancaster Amish also tend to have higher mean levels of LDL-cholesterol compared to non-Amish European Caucasians (27), with much of this difference attributable to a high frequency of the R3527Q mutation in *APOB* associated with familial hypercholesterolemia (28). Whether these results generalize to other populations remains to be determined.

In conclusion, we have shown that usual levels of physical activity are associated with a decrease in the PPL response after a fat meal and may, therefore, account for some of the cardioprotective benefits attributable to exercise.

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Abbreviations:

PPL	post-prandial lipemia
CVD	cardiovascular disease
TG	triglyceride
OFTT	oral fat tolerance test
TG AUC	the triglyceride area under the curve
BMI	body mass index
LDL	low-density lipoprotein

References

1. Zilvermit DB. Atherogenesis: a postprandial phenomenon. *Circulation* 1979;60(3):47385.
2. Patsch JR, Miesenbock G, Hopferwieser T, Muhlberger V, Knapp E, Dunn JK, Gotto AM, Jr., Patsch W. Relation of triglyceride metabolism and coronary artery disease. Studies in the postprandial state. *Arterioscler Thromb* 1992;12(11):1336–45. [PubMed: 1420093]
3. Groot PH, van Stiphout WA, Krauss XH, Jansen H, van Tol A, van Ramshorst E, Chin-On S, Hofman A, Cresswell SR, Havekes L. Postprandial lipoprotein metabolism in normolipidemic men with and without coronary artery disease. *Arterioscler Thromb* 1991;11(3):653–62. [PubMed: 2029503]
4. Nordestgaard BG, Benn M, Schnohr P, Tybjaerg-Hansen A. Nonfasting triglycerides and risk of myocardial infarction, ischemic heart disease, and death in men and women. *JAMA* 2007;298(3):299–308. doi: 10.1001/jama.298.3.299. [PubMed: 17635890]
5. Bansal S, Buring JE, Rifai N, Mora S, Sacks FM, Ridker PM. Fasting compared with nonfasting triglycerides and risk of cardiovascular events in women. *JAMA* 2007;298(3):309–16. doi: 10.1001/jama.298.3.309. [PubMed: 17635891]
6. Lundman P, Boquist S, Samnegard A, Bennermo M, Held C, Ericsson CG, Silveira A, Hamsten A, Tornvall P. A high-fat meal is accompanied by increased plasma interleukin-6 concentrations. *Nutr Metab Cardiovasc Dis* 2007;17(3):195–202. doi: 10.1016/j.numecd.2005.11.009. [PubMed: 17367705]
7. Nappo F, Esposito K, Cioffi M, Giugliano G, Molinari AM, Paolisso G, Marfella R, Giugliano D. Postprandial endothelial activation in healthy subjects and in type 2 diabetic patients: role of fat and carbohydrate meals. *J Am Coll Cardiol* 2002;39(7):1145–50. [PubMed: 11923038]
8. Vogel RA, Corretti MC, Plotnick GD. Effect of a single high-fat meal on endothelial function in healthy subjects. *Am J Cardiol* 1997;79(3):350–4. [PubMed: 9036757]
9. Sies H, Stahl W, Sevanian A. Nutritional, dietary and postprandial oxidative stress. *J Nutr* 2005;135(5):969–72. doi: 10.1093/jn/135.5.969. [PubMed: 15867266]
10. Peddie MC, Rehrer NJ, Perry TL. Physical activity and postprandial lipidemia: are energy expenditure and lipoprotein lipase activity the real modulators of the positive effect? *Prog Lipid Res* 2012;51(1):11–22. doi: 10.1016/j.plipres.2011.11.002. [PubMed: 22123195]
11. Mitchell BD, McArdle PF, Shen H, Rampersaud E, Pollin TI, Bielak LF, Jaquish C, Douglas JA, Roy-Gagnon MH, Sack P, et al. The genetic response to short-term interventions affecting cardiovascular function: rationale and design of the Heredity and Phenotype Intervention (HAPI) Heart Study. *Am Heart J* 2008;155(5):823–8. doi: 10.1016/j.ahj.2008.01.019. [PubMed: 18440328]
12. Westerterp KR. Physical activity assessment with accelerometers. *Int J Obes Relat Metab Disord* 1999;23 Suppl 3:S45–9. [PubMed: 10368002]

13. Rampersaud E, Mitchell BD, Pollin TI, Fu M, Shen H, O'Connell JR, Ducharme JL, Hines S, Sack P, Naglieri R, et al. Physical activity and the association of common FTO gene variants with body mass index and obesity. *Arch Intern Med* 2008;168(16):1791–7. doi: 10.1001/archinte.168.16.1791. [PubMed: 18779467]
14. O'Connell JR. Internet: <http://edn.som.umaryland.edu/mmmap/index.php> (accessed April 8, 2014).
15. Pollin TI, Damcott CM, Shen H, Ott SH, Shelton J, Horenstein RB, Post W, McLenithan JC, Bielak LF, Peyser PA, et al. A null mutation in human APOC3 confers a favorable plasma lipid profile and apparent cardioprotection. *Science* 2008;322(5908):1702–5. doi: 10.1126/science.1161524. [PubMed: 19074352]
16. Miyashita M, Burns SF, Stensel DJ. An update on accumulating exercise and postprandial lipaemia: translating theory into practice. *J Prev Med Public Health* 2013;46 Suppl 1:S3–11. doi: 10.3961/jpmph.2013.46.S.S3. [PubMed: 23412842]
17. Maraki MI, Sidossis LS. The latest on the effect of prior exercise on postprandial lipaemia. *Sports Med* 2013;43(6):463–81. doi: 10.1007/s40279-013-0046-9. [PubMed: 23580393]
18. Gill JM, Al-Mamari A, Ferrell WR, Cleland SJ, Packard CJ, Sattar N, Petrie JR, Caslake MJ. Effects of prior moderate exercise on postprandial metabolism and vascular function in lean and centrally obese men. *J Am Coll Cardiol* 2004;44(12):2375–82. doi: 10.1016/j.jacc.2004.09.035. [PubMed: 15607401]
19. Zhang JQ, Ji LL, Nunez G, Feathers S, Hart CL, Yao WX. Effect of exercise timing on postprandial lipemia in hypertriglyceridemic men. *Can J Appl Physiol* 2004;29(5):590–603. [PubMed: 15507695]
20. Teeman CS, Kurti SP, Cull BJ, Emerson SR, Haub MD, Rosenkranz SK. Postprandial lipemic and inflammatory responses to high-fat meals: a review of the roles of acute and chronic exercise. *Nutr Metab (Lond)* 2016;13:80. doi: 10.1186/s12986-016-0142-6. [PubMed: 27891165]
21. Herd SL, Lawrence JE, Malkova D, Murphy MH, Mastana S, Hardman AE. Postprandial lipemia in young men and women of contrasting training status. *J Appl Physiol* (1985) 2000;89(5):2049–56. doi: 10.1152/jappl.2000.89.5.2049. [PubMed: 11053361]
22. Hairston KG, Ducharme JL, Treuth MS, Hsueh WC, Jastreboff AM, Ryan KA, Shi X, Mitchell BD, Shuldiner AR, Snitker S. Comparison of BMI and physical activity between Old Order Amish children and non-Amish children. *Diabetes Care* 2013;36(4):873–8. doi: 10.2337/dc12-0934. [PubMed: 23093661]
23. Bassett DR, Jr., Tremblay MS, Esliger DW, Copeland JL, Barnes JD, Huntington GE. Physical activity and body mass index of children in an Old Order Amish community. *Med Sci Sports Exerc* 2007;39(3):410–5. doi: 10.1249/mss.0b013e31802d3aa7. [PubMed: 17473766]
24. Bassett DR, Schneider PL, Huntington GE. Physical activity in an Old Order Amish community. *Med Sci Sports Exerc* 2004;36(1):79–85. [PubMed: 14707772]
25. Esliger DW, Tremblay MS, Copeland JL, Barnes JD, Huntington GE, Bassett DR, Jr. Physical activity profile of Old Order Amish, Mennonite, and contemporary children. *Med Sci Sports Exerc* 2010;42(2):296–303. doi: 10.1249/MSS.0b013e3181b3afd2. [PubMed: 19927029]
26. Katz ML, Ferketich AK, Broder-Oldach B, Harley A, Reiter PL, Paskett ED, Bloomfield CD. Physical activity among Amish and non-Amish adults living in Ohio Appalachia. *J Community Health* 2012;37(2):434–40. doi: 10.1007/s10900-011-9460-9. [PubMed: 21858689]
27. Bielak LF, Yu P, Ryan KA, Rumberger JA, Sheedy PF, Turner ST, Post W, Shuldiner AR, Mitchell BD, Peyser PA. Differences in prevalence and severity of coronary artery calcification between two non-Hispanic white populations with diverse lifestyles. *Atherosclerosis* 2008;196(2):888–95. [PubMed: 17368463]
28. Shen H, Damcott CM, Rampersaud E, Pollin TI, Horenstein RB, McArdle PF, Peyser PA, Bielak LF, Post WS, Chang YP, et al. Familial defective apolipoprotein B-100 and increased low-density lipoprotein cholesterol and coronary artery calcification in the old order amish. *Arch Intern Med* 2010;170(20):1850–5. doi:10.1001/archinternmed.2010.384. [PubMed: 21059979]

Highlights

- Nonfasting TGs are associated with an increased risk of cardiovascular events.
- TG excursions increase with age and are higher in men than women.
- High usual levels of PA blunt the TG-raising effects of a high-fat meal.

Figure 1. Correlation of physical activity levels (log transformed) with age in men (blue) and women (red). $P < 0.001$ for both correlations.

Figure 2.

Correlation of TG AUC (log transformed) with age in men (blue) and women (red). $P < 0.001$ for both correlations.

Figure 3.

Association of physical activity levels with TG response (area under the curve). X-axis shows the categories of physical activity by quartile (low to high from left to right) in men (blue) and women (red). The box shows data points between the 25th and 75th percentiles, with whiskers showing more extreme values but within the 1.5 interquartile range (IQR). Outliers are depicted individually as dots.

Table 1.Characteristics (mean $\pm$ sd) of study subjects by sex.

	Men (n=366)	Women (n=305)	P-value
Age (yrs)	42 $\pm$ 13	45 $\pm$ 14	0.007
Body mass index (kg/m ²)	25.6 $\pm$ 3.2	27.7 $\pm$ 5.3	< 0.001
Fasting TG (mg/dl), median (25 th , 75 th)	53 (40, 75)	60 (42, 93)	0.04 [*]
Fasting total cholesterol (mg/dl)	203 $\pm$ 43	215 $\pm$ 48	0.003
Fasting LDL cholesterol (mg/dl)	137 $\pm$ 40	141 $\pm$ 45	0.66
Physical activity (thousand counts), median (25 th , 75 th)	467 (327, 637)	332 (242, 475)	< 0.001 [*]
Triglyceride AUC, median (25 th , 75 th)	776 (594, 1123)	678 (482, 1055)	< 0.001 [*]

^{*} Statistical analysis was performed on log transformed variables.

Table 2:

Association of selected variables with TG AUC, adjusted for age, sex, and kinship. * Standardized regression coefficients (betas) presented except for 'sex.'

Independent Variable	Standardized Beta	Adjusted p-value
Physical activity, ln(counts)	−0.094	0.017
Sex (female vs male)	−0.327	< 0.001
Age, yrs	0.275	< 0.001
LDL cholesterol, mg/dl	0.183	< 0.001
ln(BMI, kg/m ²)	0.399	< 0.001
ln(cholesterol, mg/dl)	0.191	< 0.001
ln(Baseline TG, mg/dl)	0.916	< 0.001

* age adjusted for sex and kinship only, and sex adjusted for age and kinship only.

Table 3.

Multivariate regression analysis of TG response (log transformed) to a high-fat challenge with physical activity. Age, sex and kinship were included as covariates in all the statistical models. Standardized regression coefficients (betas) presented except for 'sex.'

Independent Variable	Model 1			Model 2			Model 3		
	Standardized Beta	Adjusted p-value*		Standardized Beta	Adjusted p-value*		Standardized Beta	Adjusted p-value*	
Physical activity, ln(counts)	-0.094	0.017		-0.084	0.019		-0.106	0.003	
Ln(BMI, kg/m ²)				0.397	<0.001		0.383	<0.001	
Fasting LDL-C, mg/dl							0.163	<0.001	