HHS Public Access

Author manuscript

Med Sci Sports Exerc. Author manuscript; available in PMC 2017 January 01.

Published in final edited form as:

Med Sci Sports Exerc. 2016 January ; 48(1): 1–6. doi:10.1249/MSS.0000000000000740.

The Effect of Atorvastatin on Habitual Physical Activity among Healthy Adults

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Abstract

Purpose—Statin therapy can result in muscle pain, cramps, and weakness that may limit physical activity although reports are mixed. We conducted a randomized control trial to examine the effect of atorvastatin on habitual physical activity levels among a large sample of healthy adults.

Methods—Participants (n=418) were statin-naïve adults [44.0±16.1yr (X±SD)] that were randomized and double-blinded to 80mg per day of atorvastatin or placebo for 6 months. Accelerometers were worn for 96hr before and after drug treatment. Repeated measures analysis tested physical activity levels after versus before drug treatment among groups with age and VO_2max as covariates.

Results—Among the total sample, sedentary behavior increased (19.5±5.1min·d^{-1}), while light (9.1±3.0min·d^{-1}) and moderate intensity (9.7±2.8min·d^{-1}) physical activity decreased, as did total activity counts (17.8±6.3·d^{-1}×10^{-3}) over 6 months (P<0.01), with no differences between groups. The atorvastatin group increased sedentary behavior (19.8±7.4min·d^{-1}), and decreased light (10.7±4.3min·d^{-1}) and moderate (8.5±4.0min·d^{-1}) intensity physical activity (P<0.05); while the placebo group increased sedentary behavior (19.2±7.1min·d^{-1}), and decreased moderate intensity (11.0±3.8min·d^{-1}) and total physical activity counts (−23.8±8.8×10^{-3}·d^{-1}) (p<0.05).

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Disclosures: Dr. Thompson reports receiving research grants from the National Institutes of Health (grant number NIH-R44 GM085201-04), GlaxoSmithKline (protocol number LPL100601), Anthera (protocol number AN-CVD2233), B. Braun, Genomas (grant number NIH-R44 GM085201-04), Roche (protocol number NC20971), Aventis, Novartis (protocol number CPJMR0032103), and Furiex (protocol number PPD10558-010); serving as a consultant for AstraZeneca, Furiex, Regeneron, Merck, Roche, Genomas, Abbott, Lupin, Runners World, Genzyme, Sanofi, Pfizer, and GlaxoSmithKline; receiving speaker honoraria from Merck, Pfizer, Abbott, AstraZeneca, GlaxoSmithKline, and Kowa; owning stock in General Electric, JA Wiley Publishing, J&J, Sanofi-Aventis, and Abbott; and serving as a medical legal consultant on cardiac complications of exercise, statin myopathy, tobacco, ezetimibe, and nonsteroidals. The other authors have no conflicts of interest to disclose.

The results of the present study do not constitute endorsement by ACSM.

Conclusion—Time being sedentary increased and physical activity levels decreased among the total sample over 6 months of drug treatment, independent of group assignment. Our results suggest that statins do not influence physical activity levels any differently than placebo, and the lack of inclusion of a placebo condition may provide insight into the inconsistencies in the literature.

Keywords

Statins; fitness behavior; objective activity measure; accelerometer

INTRODUCTION

Hydroxy-methyl-glutaryl (HMG) CoA reductase inhibitors, or statins, are the most widely prescribed and most effective (12) medications for the treatment of dyslipidemia. However, statin therapy is associated with an increased risk of myalgia or “muscle pain”, muscle cramps, and muscle weakness that may affect medication adherence and activities of daily living (31). The true incidence of myalgia is not known, however, estimates indicate that myalgia may occur in 1% of patients in pharmaceutical trials (17) to 10–25% of patients in non-industry funded trials (7,24,26). When reported by patients on statin therapy, the symptoms of myalgia seem to appear more frequently during and after physical activity (9,18,19,29).

On average, statins can lower low density lipoprotein (LDL) cholesterol concentration by 32.4 $mg \cdot dL^{-1}$ which decreases the risk of ischemic heart disease events by about 60% and stroke by 17% (16). Despite the effectiveness of statins, only 26% of patients are currently achieving optimal LDL levels (<100 $mg \cdot dL^{-1}$) as defined by the National Cholesterol Education Program Adult Treatment Panel III (ATP III) (22). Accordingly, the American College of Sports Medicine (ACSM) recommends the following exercise prescription for the prevention, treatment, and control of dyslipidemia: moderate intensity exercise for 30 $min \cdot d^{-1}$ on ≥5 $d \cdot wk^{-1}$, or vigorous intensity exercise for 20 $min \cdot d^{-1}$ for 3 or more $d \cdot wk^{-1}$, or some combination of the two (25).

Recent support for the importance of a physically active lifestyle to prevent, treat, and control dyslipidemia are found in a cohort study conducted by Kokkinos et al. (15) examining the interactive effects of physical fitness and statin use on mortality risk among 10,043 veterans (mean age 58yr) with dyslipidemia. They found that all-cause mortality risk for individuals treated with statins was lower (18.5%) compared to those not on statins (27.5%). In patients taking statins, Cox proportional hazard models displayed that highly fit individuals (>9 metabolic energy equivalents, [METs]) had a hazard ratio of 0.3, while the least fit (≤5 METs) patients had a hazard ratio of 1.0 (15). A decreased risk of mortality in highly versus poorly fit individuals using statins reinforces the notion of the importance of engaging in habitual physical activity for the prevention, treatment, and control of dyslipidemia.

To the best of our knowledge, Bruckert et al. (7) and Lee et al. (17) have conducted the only studies examining habitual physical activity levels among individuals receiving statin therapy. Bruckert et al. (7) enrolled 7,924 participants with hyperlipidemia and compared

non-symptomatic and symptomatic statin user's physical activity levels. Symptomatic participants were generally more active than non-symptomatic participants. Nevertheless, 38% of participants, regardless of their symptomatology, reported that their muscular symptoms prevented moderate exertion during everyday activities (7). These findings suggest that patients on statins who experience myalgia may compensate for their symptoms by limiting daily physical activity. However, in this cross-sectional study design changes in physical activity levels before versus after drug treatment were not evaluated.

Lee et al. (17) examined longitudinal changes of physical activity levels in statin users vs a placebo control over an average of 6.9 yr in 3,039 men >65 yr using the Physical Activity Scale for the Elderly (PASE; baseline and two months) and accelerometers (4–7 yr after baseline). Of these, 727 (24%) were prevalent statin users, 1,467 (48%) were statin naïve, and 845 (28%) were *new* statin users. Self-reported physical activity decreased in a similar fashion in all three groups. Furthermore, statin users expended less daily METS (−0.03), spent less time in moderate ($-5.4\ \text{min}\cdot\text{d}^{-1}$) and vigorous ($0.6\ \text{min}\cdot\text{d}^{-1}$) activity, and increased ($0.6\ \text{min}\cdot\text{d}^{-1}$) sedentary behavior compared to non-statin users as measured by accelerometer. The authors concluded that accelerometers showed statin use is associated with modestly lower physical activity, and PASE scores showed *new* statin users had a more rapid decline in physical activity than nonusers. However, the objective measure (accelerometer) only measured physical activity at one time point to compare groups and did not measure physical activity before and after statin use.

To date, there has not been a randomized controlled trial that examined physical activity levels using objective measurements before and after statin use compared to placebo. Therefore, we randomized healthy men and women from 20 to 76 yr to 80mg of atorvastatin or placebo to determine the effect of statins on habitual physical activity levels as measured by accelerometer before and after drug treatment for 6 months. We hypothesized that overall physical activity levels as measured by accelerometer would decrease in the drug treatment group compared to the placebo group.

METHODS

Data for this study were derived from a larger project funded by the National Institutes of Health (NIH) (1R01HL081893-01A2) entitled: *The Effect of Statins on Skeletal Muscle Function and Performance*. The primary purpose of this larger study was to investigate the incidence of statin-induced muscle complaints and determine the effect of statins on skeletal muscle strength, endurance, and cardiorespiratory fitness (23,32). Only the methods pertinent to this sub-study will be detailed below.

Participants

Approximately 420 participants were enrolled across the three test sites, with an equal number of men and women recruited into 20–39, 40–54, and 55+ yr age groups. Participants were recruited via newspaper advertisements in local and campus papers, flyers, posters, and classroom announcements. IRB approval was obtained at each of the participating institutions. Prior to enrollment in the study, all participants were required to complete an informed consent.

Participants were excluded from the study if they had a history of cancer within the previous 5 yr; hyper- or hypothyroidism; or diagnosed coronary artery disease, peripheral vascular disease, or diabetes mellitus, all of which warrant immediate initiation of lipid-lowering therapy (22). Participants with hepatic disease (Alanine Aminotransferase >2X upper limit of normal) or renal disease (serum creatinine >2mg·L^{-1}) were excluded, as these conditions could limit statin metabolism and excretion. Participants deemed "statin survivors" who had previously tolerated statin therapy, those on concomitant therapy known to affect statin metabolism, and anyone with an injury or condition that would limit exercise, including cardiac ischemia as determined by the Bruce protocol treadmill test, were excluded. Participants with a Framingham 10-yr risk of >20%, those currently controlled on antihypertensive medications (blood pressure [BP] <140/90 mmHg), and Creatine Kinase (CK) values <10X ULN were eligible for enrollment. Physical activity level at baseline was not an inclusion or exclusion criteria for enrollment. However, we did instruct participants not to intentionally change their physical activity habits throughout the study.

Procedures

Baseline measurements were collected at visit one and two using standard procedures (33). Visit one included measurements of height, weight, body mass index (BMI), waist circumference (WC), BP, and heart rate (HR), and a fasted blood draw. Visit two occurred a minimum of 72 hr after visit one and included a Balke protocol graded maximal treadmill test to determine participants' VO_2max (mL·kg^{-1}·min^{-1}) and distribution of an accelerometer to measure physical activity levels. Participants returned the accelerometer approximately four days later at visit three where they were randomized to either 80mg per day of atorvastatin or placebo.

During visit five 6 months after study enrollment, participants completed a blood draw, graded maximal treadmill test, had BP measured, and were given an accelerometer. Approximately four days later (visit six), participants returned the accelerometer and remaining study medication was collected and counted to assess adherence over the previous 6 months.

Blood Specimen Collection

A blood sample was collected prior to (visit one) and 6 months after (visit five) randomization to the study drug treatment group. Analyses included: thyroid stimulating hormone, creatine kinase, serum creatinine, and alanine aminotransferase levels to verify subject eligibility and to determine safety of taking a statin. Lipid levels, including total cholesterol (mg·dL^{-1}), LDL cholesterol (mg·dL^{-1}), high density lipoprotein cholesterol (HDL) (mg·dL^{-1}), and triglycerides (TG) (mg·dL^{-1}) were also analyzed, while preserving double blinding of the study drug groups.

Anthropometric Measurements

Participants' anthropometric measurements included measurement of height, weight, BMI, and WC (33). A wall-mounted measuring tape was used to record participants' height (cm). Weight was measured using a calibrated balance beam scale, and recorded in kg. Height and weight measurements were used to calculate BMI (kg·m^{-2}). WC (cm) was measured with a

non-distensible Gulick tape measure at the narrowest part of the subject's torso when participants were standing in a relaxed position.

Systolic (SBP) and diastolic (DBP) BP (mm Hg) were measured by auscultation with a sphygmomanometer (Trimline™, PyMaH Corp., Somerville, NJ, USA), BP cuff (Omni Kuff®, Latex Free, Universally connection BALANCED® design, Trimline Medical Products, Somerville, NJ, USA), and stethoscope (3M™ Litman® Lightweight II SE, St. Paul, MN, USA) using standard procedures (33). Participants remained seated with both feet flat on the floor, legs uncrossed, and back supported for several minutes before BP was recorded using the non-dominant arm. A HR monitor (Polar Vantage NV™ HR Monitor, Polor Electro Inc., Port Washington, NY, USA) was used to record participants' resting HR ($b \cdot min^{-1}$).

Maximal Graded Exercise Test

A graded maximal treadmill test using the Balke protocol (4) was utilized to determine participants' VO_2max ($mL \cdot kg^{-1} \cdot min^{-1}$). Participants began by walking at a 2 mph pace on a 0% incline for 2 min, after which investigators increased the treadmill speed until it reached a level that participants could maintain for at least 30 min. The treadmill grade was then raised by 1% every minute until test completion. Participants wore a respiratory apparatus (Parvomedics TrueOne 2400 metabolic cart, Parvomedics Corp, Sandy, UT, USA) during the treadmill test, which was used to analyze expired oxygen and carbon dioxide via a breath-by-breath collection method to determine baseline VO_2max. Absolute indications for terminating the exercise test (33) included: a drop in SBP of >10 mmHg from baseline SBP despite an increase in workload with evidence of ischemia, moderately severe angina (3 on standard scale), increasing nervous system symptoms (e.g., ataxia or dizziness), signs of poor perfusion, technical difficulties, subject's desire to stop, sustained ventricular tachycardia, and an ST elevation (+1.0 mm) in leads without diagnostic A-waves (other than V_1 of aVR).

Accelerometer

An Actical® accelerometer (1) measured physical activity levels before and after subjects were randomized to the drug treatment groups. Participants were instructed to wear the device for 96 consecutive hours (four days), including two weekdays and two weekend days. Accelerometers were worn on the waistband or belt via a hip clip, and only removed while sleeping and bathing.

Accelerometers recorded physical activity in 25-sec epochs. Recording began immediately after participants left the laboratory. At least 96 hr later, participants returned the accelerometer to investigators. If the device did not adequately record the participant's physical activity over 96 hr, the participant was asked to wear the accelerometer for another 96 consecutive hours. Accelerometers recorded several parameters of participants' physical activity including activity counts (d^{-1}), time spent in a sedentary state ($min \cdot d^{-1}$) and engaging in light ($min \cdot d^{-1}$), moderate ($min \cdot d^{-1}$), and vigorous intensity activity ($min \cdot d^{-1}$).

Statistical Analysis

An independent samples t-test was used to compare baseline subject characteristics between the atorvastatin and placebo groups. These characteristics included baseline anthropometric measurements (height, weight, BMI, WC), serum lipid levels (TC, LDL, HDL, TG), VO_2max, BP, HR, and age. An independent samples t-test was also used to determine any differences in physical activity levels between groups collected by accelerometer. Accelerometer variables included time spent sedentary ($min \cdot d^{-1}$), and time spent engaging in light, moderate, and vigorous intensity physical activity ($min \cdot d^{-1}$) as well as total activity counts (d^{-1}).

Repeated measures analysis of covariance tested whether participants' physical activity levels differed over 6 months among the overall sample and by drug treatment with gender and season as a fixed factors and age, BMI, WC, VO_2max, and change in CK as covariates. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) 14.0 for Windows (SPSS Inc, Chicago, IL), and $P<0.05$ was established as the level of statistical significance.

RESULTS

Participant Characteristics

The sample for this sub-study (n=418) primarily comprised of healthy, middle aged Caucasian (93.7%), non-Hispanic (95.4%) women (51.7%) and men (48.3%). Participants were overweight, had above optimal LDL (22), and had normal BP, HDL, total cholesterol, and TG. Participants' baseline VO_2max indicated that men were borderline average regarding their cardiorespiratory fitness level and women were above average for people of their age (25). There were no significant differences among participant characteristics by treatment group (Table 1).

Effect of Atorvastatin on Physical Activity—At baseline, participants exceeded the current United States Department of Health and Human Services (USDHHS) recommendations for daily physical activity, by participating in >2 hr of moderate intensity physical activity daily on average (Table 2) [35]. Participants in both drug groups reported spending most of their time being sedentary (>17 $hr \cdot d^{-1}$), followed by time spent in light (~3.5 $hr \cdot d^{-1}$) and moderate (~2 $hr \cdot d^{-1}$) intensity physical activity, and the least amount of time spent in vigorous (<10 $min \cdot d^{-1}$) intensity physical activity. Time spent in each of the four physical activity categories and activity counts (d^{-1}) at baseline were not different by treatment group (Table 2).

Changes in physical activity levels over the 6 month study are presented in Table 3. Among the total sample over the 6 month study duration, time spent being sedentary increased ($P < 0.001$), time spent in light ($P = 0.002$) and moderate intensity ($P = 0.001$) physical activity decreased, as did activity counts ($P = 0.006$). Time spent in vigorous intensity physical activity decreased, but this change did not achieve statistical significance ($P = 0.053$; Table 3). In these primary statistical analyses, there were no statistically significant differences in physical activity levels between group differences ($P > 0.05$); nonetheless, we performed

subgroup analyses to more completely depict the physical activity profiles of each group and address our research question. Accordingly, the atorvastatin group increased time spent being sedentary ($P = 0.010$), and decreased time spent in light ($P = 0.017$) and moderate ($P = 0.038$) intensity physical activity. The placebo group increased time spent being sedentary ($P = 0.006$), and decreased time spent in moderate intensity ($P = 0.005$) and total physical activity counts ($P = 0.022$). The placebo group also decreased time spent in light intensity activity, but this change was not statistically significant ($P = 0.067$; Table 3).

DISCUSSION

The purpose of this study was to determine if statins adversely affect habitual physical activity levels among healthy individuals. Surprisingly, we found a similar reduction in overall physical activity levels in both the atorvastatin (−6.6 $min \cdot d^{-1}$) and placebo (−6.4 $min \cdot d^{-1}$) groups after 6 months of treatment. The atorvastatin group increased sedentary time (19.8 $min \cdot d^{-1}$) and decreased time spent in light (−10.7 $min \cdot d^{-1}$) and moderate intensity physical activity (8.5 $min \cdot d^{-1}$), while the placebo group increased sedentary time (19.2 $min \cdot d^{-1}$) and decreased time spent in moderate intensity physical activity (−11.0 $min \cdot d^{-1}$) and total activity counts (−23.8 $d^{-1} \times 10^3$). This study is the first randomized control trial to measure habitual physical activity levels before and after 6 months of statin therapy among healthy adults. Our results suggest that patients with dyslipidemia should be encouraged to be and continue to be physically active when on a statin regimen, as we found no differences in physical activity levels between treatment groups over the 6 months duration of the study. These findings and those of Kokkinos et al. (13,14) indicate that physical activity should be encouraged as lifestyle therapy in conjunction with statins as pharmacological therapy for the prevention, treatment, and control of dyslipidemia as well as decreased mortality in a population that is at increased risk for CVD (22).

There may be several reasons that account for our finding that the placebo and drug treatment groups similarly decreased their physical activity levels over the 6 month duration of the study. First, the seasons in which the subjects participated may have contributed since the study spanned 3 years, had rolling enrollment, and was conducted in New England in which there are four seasons. Therefore, we examined the seasons in which the subjects participated as a fixed factor in our statistical analyses and found season not to exert any statistically significant effects on the findings. Second, the subjects may have experienced an alerting reaction to wearing the accelerometer for the first time prior to randomization to drug treatment group which could account for the decreases in physical activity pre- to post-treatment that we observed (2,3). However, accelerometers have demonstrated test-retest reliability (11,20), and therefore, a decline in physical activity levels due to the alerting reaction of initially wearing the accelerometer was not likely to occur or explain our findings.

Third, there may have been a psychological fear of medication side-effects (10) leading to the decreased physical activity levels shown in both groups. Subjects were informed during the consent process that myalgia is a potential side-effect of taking statins and that it is often increased by exercise, a disclosure that may have caused them to decrease their physical activity levels during the study. However, this possibility appears unlikely because both

groups continued to exceed the USDHHS recommendations of 60 minutes of moderate intensity, physical activity per day over 6 months of study participation. Last, the decreases we observed in physical activity may have simply been a regression to the mean over the 6 month duration of the study among a relatively healthy, physically active population (21,28). Nonetheless, despite the similar decreases in physical activity in both drug treatment groups, as previously stated study participants still continued to exceed (122.2 $min \cdot d^{-1}$) the USDHHS-recommended 60 minutes of daily, moderate intensity physical activity over the 6 month study period (35).

Our results are in contrast to other investigative teams that have examined the effect of statins on physical activity. Sirvent et al. (30) measured VO_2max in asymptomatic and symptomatic patients treated with statins and a group of controls and found that VO_2max was significantly lower in the patients treated with statins than in the controls. Their results suggested that patients taking statins may develop exercise intolerance which could limit physical exercise and daily physical activities to avoid symptoms of myopathy. In addition, Bruckert et al. (7) indicated that 38% of patients receiving high-dosage statin therapy in a usual care setting reported that their muscular symptoms prevented moderate exertion during everyday activities; again, suggesting that subjects may have compensated for their statin associated muscular symptoms by limiting daily physical activity. Lee and colleagues (17) were the only other researchers to use accelerometers to examine the effect of statins on physical activity and found that statin users decreased their self-reported physical activity over time significantly more than non-statin users. Approximately 12% (7) and 50% (30) of the subject population taking statins in the studies by Sirvent et al. (30) and Brucket et al. (7) had myalgia symptoms compared to only 7% of symptomatic subjects in our sample (23). The lesser prevalence of muscle complaints in our study compared to theirs as well as our study sample being younger may have contributed to the differences in our findings. However, the most likely explanation is the differences in our study designs; with ours being a double-blinded, randomized control trial, whereas the others (7,17,30) were largely cross-sectional analyses without an objective measurement of physical activity before and after statin use.

This sub-study was limited by several factors. Data collection occurred at multiple sites, which introduced the possibility of site/interpreter bias. However, a standard protocol for data collection was used, and the researchers attended monthly meetings to discuss study progression to minimize the possibility of bias and errors. Also, the study population was self-selected and did not include subjects deemed to be “unhealthy” due to several possible co-morbidities or health conditions. Therefore, the study population did not represent the population that is typically prescribed statin therapy (i.e., patients with dyslipidemia or other conditions associated with CVD). Nonetheless, we utilized a high dose of atorvastatin (i.e., 80mg) that would be more likely to elicit myalgia symptoms than lower doses. Additionally, we performed a subanalysis that showed participants with myalgia symptoms decreased time spent in vigorous activity ($P = 0.008$). However, given the small sample of subjects with myalgia (n=28), these findings should be interpreted with caution. Strengths of the current study included a double-blind, randomized control trial design with a large sample size

across the lifespan. Data were collected using accelerometers which are considered the objective gold-standard measure of physical activity in large population studies such as ours.

In summary, the results from this double-blinded, randomized control trial found that the physical activity levels of participants taking high dose atorvastatin compared to study participants taking placebo were not different, as both groups decreased time spent being physically active and increased the amount of time spent being sedentary over the 6 month study period. Season in which the subjects participated in the study, sensitivity to initially wearing the accelerometers, and regression to the mean in a physically active subject population are possible but unlikely explanations for our findings. Our findings reinforce the notion of the importance of maintaining a physically active lifestyle while on statin therapy for the prevention, treatment and control of dyslipidemia as well as the protective effects of both physical fitness level and statin therapy on mortality from CVD (15). Nevertheless, future studies should examine the effects of an exercise intervention that conforms to the recommendations for those with dyslipidemia (25) before and after the initiation of varying doses of statin therapy among individuals with dyslipidemia who are initially sedentary to better represent the patient population and conditions under which myalgia symptoms would appear, if at all.

Acknowledgments

We would like to recognize Dr. Priscilla M. Clarkson for her great contributions to the STOMP study.

The current study was supported by National Institutes of Health grant # 5R01HL081693-4. Dr. Thompson reports receiving research grants from the National Institutes of Health (grant number NIH-R44 GM085201-04), GlaxoSmithKline (protocol number LPL100601), Anthera (protocol number AN-CVD2233), B. Braun, Genomas (grant number NIH-R44 GM085201-04), Roche (protocol number NC20971), Aventis, Novartis (protocol number CPJMR0032103), and Furiex (protocol number PPD10558-010); serving as a consultant for AstraZeneca, Furiex, Regeneron, Merck, Roche, Genomas, Abbott, Lupin, Runners World, Genzyme, Sanofi, Pfizer, and GlaxoSmithKline; receiving speaker honoraria from Merck, Pfizer, Abbott, AstraZeneca, GlaxoSmithKline, and Kowa; owning stock in General Electric, JA Wiley Publishing, J&J, Sanofi-Aventis, and Abbott; and serving as a medical legal consultant on cardiac complications of exercise, statin myopathy, tobacco, ezetimibe, and nonsteroidals. The other authors have no conflicts of interest to disclose. The results of the present study do not constitute endorsement by ACSM.

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Table 1

Participant characteristics for baseline anthropometrics, cardiorespiratory fitness, and lipid measures.

	Total Sample (*N*=418)	Atorvastatin (*N*=201)	Placebo (*N*=217)
Age (yr)	44.0 ± 16.1	43.7 ± 15.7	44.2 ± 16.5
Height (m)	1.7 ± 0.1	1.7 ± 0.1	1.7 ± 0.1
Weight (kg)	78.0 ± 16.8	76.8 ± 15.6	79.1 ± 17.9
BMI ($kg \cdot m^{-2}$)	26.3 ± 4.7	26.5 ± 4.6	26.1 ± 4.7
Waist Circumference (cm)	86.2 ± 13.9	86.6 ± 12.9	85.7 ± 14.7
Systolic Blood Pressure (mm Hg)	118.8 ± 13.3	118.8 ± 12.7	118.8 ± 13.8
Diastolic Blood Pressure (mm Hg)	75.2 ± 9.6	75.6 ± 9.1	74.9 ± 10.1
Heart Rate ($b \cdot min^{-1}$)	68.9 ± 11.3	69.9 ± 11.2	68.0 ± 11.4
VO_2max ($ml \cdot kg^{-1} \cdot min^{-1}$)	33.9 ± 9.7	33.5 ± 9.2	34.2 ± 10.2
Total Cholesterol ($mg \cdot dL^{-1}$)	196.7 ± 38.3	199.3 ± 38.3	194.2 ± 38.2
HDL Cholesterol ($mg \cdot dL^{-1}$)	58.1 ± 17.0	57.6 ± 17.9	58.7 ± 16.1
LDL Cholesterol ($mg \cdot dL^{-1}$)	117.4 ± 33.7	120.4 ± 34.6	114.6 ± 32.6
Triglycerides ($mg \cdot dL^{-1}$)	106.7 ± 55.6	108.7 ± 57.2	104.7 ± 54.2

Data are presented as mean ± SD. All values $P>0.05$

Table 2

Baseline physical activity patterns recorded by accelerometer for the total sample and by drug treatment group.

Variable	Total Sample (n=418)	Atorvastatin (n=201)	Placebo (n=217)
Sedentary Behavior ($min \cdot d^{-1}$)	1098.0 ± 98.7	1093.7 ± 99.6	1101.8 ± 98.0
Light Intensity ($min \cdot d^{-1}$)	206.9 ± 59.4	208.3 ± 58.0	205.6 ± 60.9
Moderate Intensity ($min \cdot d^{-1}$)	131.1 ± 51.5	134.3 ± 54.0	128.2 ± 49.0
Vigorous Intensity ($min \cdot d^{-1}$)	3.7 ± 7.8	3.3 ± 6.4	4.1 ± 8.9
Counts ($d^{-1} \times 10^3$)	191.3 ± 7.0	185.7 ± 6.9	196.3 ± 11.7

Data are presented as mean ± SD. All values $P>0.05$

Table 3

Absolute change in physical activity for the total sample and by drug treatment group from baseline to 6 months recorded by accelerometer.

	Total Sample (n=418)		Atorvastatin (n=201)		Placebo (n=217)		Drug Difference
Variable	**Baseline**	**Δ at 6 Months**	**Baseline**	**Δ at 6 Months**	**Baseline**	**Δ at 6 Months**	**Δ Atorvastatin −Δ Placebo**
Sedentary (min·d^{-1})	1096.9 ± 4.9	19.5 ± 5.1***	1092.7 ± 7.2	19.8 ± 7.4**	1101.1 ± 6.7	19.2 ± 7.1**	0.6 ± 10.3
Light Intensity (min·d$^{-1)}$	207.3 ± 2.9	−9.1 ± 3.0**	208.5 ± 4.2	−10.7 ± 4.3*	205.9 ± 4.2	−7.5 ± 4.1	−3.1 ± 6.0
Moderate Intensity (min·d^{-1})	131.9 ± 2.5	−9.7 ± 2.8***	135.1 ± 3.8	−8.5 ± 4.0*	128.7 ± 3.3	−11.0 ± 3.8**	2.5 ± 5.6
Vigorous Intensity (min·d^{-1})	3.7 ± 0.3	−0.6 ± 0.3	3.4 ± 0.4	−0.5 ± 0.4	4.0 ± 0.5	−0.6 ± 0.4	0.1 ± 0.6
Counts (d^{-1}×10^3)	192.2 ± 6.5	−17.8 ± 6.3**	187.2 ± 6.0	−11.7 ± 9.2	196.6 ± 11.1	−23.8 ± 8.8*	12.0 ± 12.8

Data are presented as mean ± SD.

* $P < 0.05$,

** $P < 0.01$,

*** $P < 0.001$, adjusted for age and VO_2max