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## Case Report

### Effect of Exercise Volume on HDL-Cholesterol: A 7-Year Case Study

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#### Abstract

**Introduction:** While exercise is known to increase HDL-cholesterol, it is not known if larger exercise volumes produce larger increases in HDL. However, the range of exercise volumes used in most training studies is limited. This report presents a case study of a middle-aged male who engaged in large variations of exercise volume over 7 years while frequently measuring HDL. The purpose was to determine if large increases in exercise volume were associated with larger increases in HDL than previously reported.

**Methods:** The subject maintained detailed logs of his main form of exercise, bicycling. These logs were analyzed to determine the average distance cycled per week over the 8 weeks preceding each HDL measurement. A retrospective comparison of cycling distance and HDL was conducted on 6 ½ years of data. Then, the subject intentionally altered cycling distance to prospectively examine its effect on serum HDL in the subsequent 6 months.

**Results:** The subject averaged 58 to 585 km of bicycling per week over 8-week periods, which was estimated to be approximately 1,000-10,000 kcal.wk<sup>-1</sup> of net energy expenditure. HDL varied from 50 to 84 mg.dL<sup>-1</sup>, and a strong positive relationship with exercise volume was observed during both the retrospective and prospective portions of the study.

**Conclusion:** Large increases in exercise volume were associated with large increases in HDL in a middle-aged male subject. These results suggest that the modest increases in HDL in most training studies may be due to the small exercise volume used.

**Keywords:** Energy Expenditure; Heart Disease; High-Density Lipoprotein; Low-Density Lipoprotein

#### Introduction

Regular exercise is known to increase plasma High-Density Lipoprotein (HDL) cholesterol in those with and without coronary heart disease [1-3]. The volume of exercise performed on a weekly basis might be expected to have an influence on the amount of HDL increase, but this has not yet been established. The volume of exercise can best be described as the net energy expenditure (caloric consumption above that needed for rest), and can be determined from intensity x duration x frequency of exercise. Cross-sectional studies of runners, in which distance run per week serves as an effective measure of volume, suggest a volume effect on HDL. Williams found a dose-response, in that mean HDL values ranged from 60 to 68 mg.dL<sup>-1</sup> among women whose typical running ranged from less than 16 km to more than 64 km per week [4]. In males, HDL values for the same running distances ranged from

48 to 57 mg.dL<sup>-1</sup> [5]. Further, Williams analyzed the volume and intensity (speed) of running among these cohorts and concluded that the effect of volume was 6 times greater than that of intensity [6]. While cross-sectional studies establish relationships between variables, they are unable to establish cause and effect.

Reviews of training studies support the lack of an intensity effect on HDL [2,7]. However, a major review of training studies was also unable to establish a volume effect of exercise on HDL [2]. Training studies usually report small increases (4-9%) in HDL following a few weeks or months of exercise, but the volume of training is generally small, typically around 1,000 kcal.wk<sup>-1</sup> and rarely more than 2,000 kcal.wk<sup>-1</sup> [1,2]. Rarely have researchers compared more than one exercise training volume in the same investigation. One group compared a gross energy expenditure of 1,200 versus 2,000 kcal.wk<sup>-1</sup> and found significant increases in HDL primarily in the higher volume group [8,9]. It was hypothesized in the current study that an individual who experienced large increases and decreases in exercise volume would demonstrate

larger increases and decreases in HDL than shown in most training studies.

## Methods

An adult male who bicycled as his main form of exercise kept detailed journals of his riding history over a 7-year time span (April 2000 to May 2007), during which his lipoprotein profile was measured 14 times. His riding ranged from 0 to 1500 km in any one week, averaging 58 to 585 km per week over 8-week periods. The time required for this bicycling ranged from 0 to approximately 52 hours in any given week, or approximately 2-20 hours per week averaged over 8-week periods. He typically rode year-round, with limited volume in the fall and winter and larger volumes in the spring and summer. During periods of limited riding, he engaged in group rides of 1-2 hours' duration that included intense efforts. During periods of greater riding volume, these group rides were supplemented with rides of longer duration, 5-12 hours per ride, performed at lower intensity. In year four, he crossed the United States, averaging 212 km per day for 26 days (July 18-August 12, 2004).

Serum lipid concentrations were determined by a hospital laboratory using standard enzymatic colorimetric analysis from antecubital blood samples taken in the fasting state. On several occasions, fasting triglycerides were measured and LDL-cholesterol was calculated as total cholesterol minus (HDL-cholesterol plus triglycerides/5). The subject was 46 years and 7 months old at the time of the first HDL measurement at the start of year one. His maximal oxygen consumption was measured twice during the period of investigation using a calibrated metabolic cart ( $V_{\max}$  29c, Sensor Medics, Yorba Linda, CA); in year five, at a body mass of 66 kg, he attained 63 mL $\cdot$ min $^{-1}\cdot$ kg $^{-1}$  on a bike ergometer; in year six, at 64 kg, he attained 62 mL $\cdot$ min $^{-1}\cdot$ kg $^{-1}$  on a treadmill. While performing an ECG stress test in year six, significant ST-segment depression was observed and he was subsequently diagnosed with asymptomatic, single-vessel Coronary Artery Disease (CAD). He was treated with simvastatin (40 mg $\cdot$ d $^{-1}$ ), niacin (2 g $\cdot$ d $^{-1}$ ) and fish oil (4 g $\cdot$ d $^{-1}$ ). He has a strong family history of heart disease.

Subsequent to his diagnosis with CAD, the subject noticed that his HDL measurement was lower than usual and wondered if it might be due to a recent decrease in his exercise volume. Thus, a review of his exercise log and his HDL measurements over the previous 6 1/2 years was performed. Bicycling distance per week was averaged over the 4-, 6- and 8-week periods prior to each HDL measurement. The distance for the 8-week periods yielded the best relationship with the HDL values, and those are the data reported here.

After performing the retrospective analysis, the subject prospectively altered his exercise volume in an attempt to manipulate the HDL values. Starting from 58 km $\cdot$ wk $^{-1}$ , he engaged

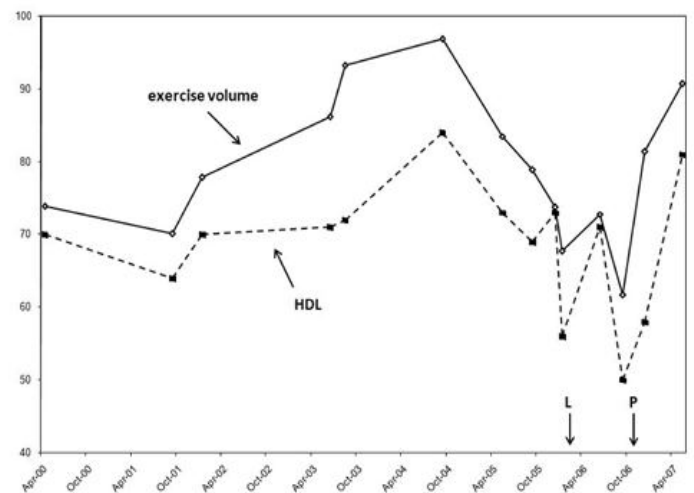
in two 8-week periods of relatively high (212 km $\cdot$ wk $^{-1}$ ) and very high (391 km $\cdot$ wk $^{-1}$ ) volume and repeated the HDL measurements.

Analysis of the subject's personal data was approved as exempt research by the university Institutional Review Board.

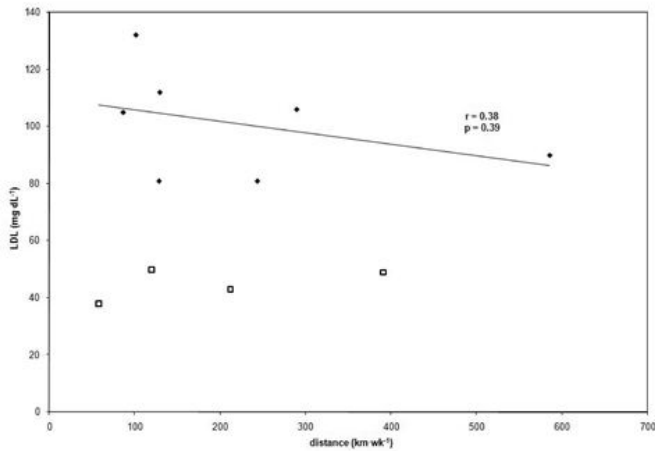
## Results

A clear relationship was observed between exercise volume and HDL that is best illustrated by expressing volume as the log of weekly bicycling distance (Figure 1). HDL ranged from 50 to 84 mg $\cdot$ dL $^{-1}$  while exercise volume ranged from 58 to 585 km $\cdot$ wk $^{-1}$ . As observed in Figure 1, increases and decreases in exercise volume during the retrospective part of the study were closely matched by corresponding increases and decreases in HDL. This relationship was confirmed during the prospective part of the study by increasing exercise volume from 58 to 391 km $\cdot$ wk $^{-1}$  (a 6.7-fold increase), which resulted in HDL rising from 50 to 81 mg $\cdot$ dL $^{-1}$  (a 62% increase). A linear regression of HDL versus log [km $\cdot$ wk $^{-1}$ ] yielded a correlation of 0.78, with  $p = 0.001$  (regression not displayed). While lipid therapy substantially reduced the subject's LDL values (see below), it had no discernible effect on his HDL values.

The highest HDL value of 84 mg $\cdot$ dL $^{-1}$  was recorded one month after completing a cross-country ride. The exercise volume for the 4 weeks immediately preceding the measurement was only 138 km $\cdot$ wk $^{-1}$ , while that for the preceding 4 weeks was 1033 km $\cdot$ wk $^{-1}$ , yielding an 8-week average of 585 km $\cdot$ wk $^{-1}$ . This observation suggests that the effect of exercise on HDL is maintained for several weeks.



**Figure 1:** Plot of exercise volume and HDL (mg $\cdot$ dL $^{-1}$ ) over time in the subject. Exercise volume is expressed as log of distance (km) per week, multiplied by 35 (to scale with the figure). L: lipid therapy began in February 2006. P: prospective manipulation of exercise volume began in October 2006.



**Figure 2:** Relationship of LDL to exercise volume. Closed symbols: prior to lipid therapy. Open symbols: on lipid therapy.

As seen in Figure 2, exercise volume did not have a significant effect on low-density lipoprotein (LDL) cholesterol. Lipid therapy dramatically lowered LDL, from a pre-therapy average of  $101 \pm 18$  mg dL<sup>-1</sup> to  $45 \pm 6$  mg dL<sup>-1</sup> ( $p < 0.001$  by Student t-test).

## Discussion

In a single male subject, middle-aged and with asymptomatic coronary heart disease, exercise volume had a strong, positive relationship with serum HDL-cholesterol. The range of exercise volume over the 7 years studied was enormous by usual clinical standards, ranging from approximately 2 to 20 hours per week for various 8-week periods. Given the subject's measured aerobic capacity, it is estimated that the net caloric expenditure ranged from approximately 1,000 to 10,000 kcal per week for 8-week periods (with a high of 25,000 kcal wk<sup>-1</sup> for a 3-week period).

The US Department of Health and Human Services physical activity guidelines for Americans state that the recommended volume of exercise is 2.5 hours per week at a moderate intensity (3.0-5.9 metabolic equivalents, METs) or 1.25 h wk<sup>-1</sup> at a vigorous intensity (> 6 METs) [10]. The guidelines further state that greater benefits can be obtained utilizing twice these volumes. Given the subject's fitness level (maximal capacity of 18 METs), virtually all of his exercise was performed at a "vigorous" intensity, even if long duration exercise sessions were performed at levels as low as 40% of capacity. Thus, when he averaged 20 hours per week over 8-week periods, he was performing 16 times the basic level, and 8 times the higher level, of exercise recommended by the DHHS. It is not unusual for endurance athletes to expend similar net amounts of energy as the subject in this case report. Runners in the most active cohorts of Williams' studies expended more than 4,000 kcal wk<sup>-1</sup>, and these individuals possessed the highest levels of HDL [4,5]. Athletes in the Tour de France maintain a net energy

expenditure of 21,000 kcal wk<sup>-1</sup> over three weeks of bicycle racing [11].

A major review of training studies failed to detect a volume effect of exercise on HDL, despite the fact that exercise did increase HDL [2]. There could be several reasons for this. It may be that exercise has only a modest effect in raising HDL, and once the threshold volume of exercise is attained an increase will be observed, but no further increase would then be expected with greater volumes. Alternatively, the range of volumes in the studies reviewed may have been too small to allow a dose-response to be observed. Of 44 studies in the review, only one used a gross energy expenditure greater than 2,100 kcal wk<sup>-1</sup>. Further, it is rare for individual studies to examine more than one volume and make direct comparisons. When this has been done, the higher volume was superior in raising HDL [8,9]. However, the increase in HDL was modest (3-4 mg dL<sup>-1</sup> on average), as was the volume of the higher volume group (gross energy expenditure of 2,000 kcal wk<sup>-1</sup>).

In analyzing the subject's exercise logs it was found that averaging exercise volume over 8-week periods provided a closer relationship to HDL than over 4- or 6-week periods. This was most dramatically illustrated by the finding that the highest HDL measurement (84 mg dL<sup>-1</sup>) followed a 4-week period of relatively low volume (138 km wk<sup>-1</sup>) but an 8-week period of high volume (585 km wk<sup>-1</sup>). Slentz et al. found that a significant increase in HDL following training was maintained during 15 days of detraining [9]. Based on the results in the current subject, the effect of exercise on HDL may last even longer than the 2 weeks examined by Slentz et al.

The mechanism by which chronic exercise results in an increase in HDL is not fully understood, but several possibilities exist. Durstine and Haskell proposed an exercise-induced increase in enzymatic pathways associated with reverse cholesterol transport [12]. Slentz et al. suggested that decreased fat stores and increased skeletal muscle mitochondria caused by training would alter HDL metabolism [9]. A recent review by Marques et al. provides more details, including an increase in lecithin-cholesterol acyltransferase activity, and increased hepatic gene expression of PPAR-alpha and ABCA1 [13]. In addition to the increase in HDL, numerous other positive cardiovascular benefits have been attributed to exercise training, and a volume effect has been acknowledged in the 2018 Physical Activity Guidelines from the US Department of Health and Human Services. This volume effect has largely been attributed to cross-sectional epidemiological studies [14,15]. Thus, additional clinical trials are needed.

The results of the current study are derived from a single subject, which is a major limitation. This subject may have an unusual serum HDL response to exercise and thus not be reflective of what other individuals may expect if they were to engage in

similarly high volumes of exercise. Measurements of serum lipids were not performed at regular intervals or in a systematic way, such as in association with prescribed changes in exercise frequency, intensity, and duration. Moreover, it is possible that other factors besides exercise affected the subject's HDL values over the 7-year time span studied. However, the cross-sectional data that Williams derived from distance runners [4-6] supports the concept that large exercise volume may cause very high HDL values.

## Conclusion

Exercise volume appears to have a pronounced effect on HDL that is not apparent from training studies that use relatively small volumes of exercise. The volume effect on HDL exhibited by the subject in the current study may reflect an unusual individual response, but these results suggest further investigation regarding the optimal amounts of exercise for maximizing HDL is warranted. Most clinical trials designed to examine the effect of exercise on HDL have had subjects perform only 1,000-2,000 kcal of exercise per week, requiring about 2-3 hours of moderate-intensity aerobic exercise. Studies are needed that double and triple that volume of exercise, to determine if larger numbers of individuals in a controlled, supervised setting will experience significantly greater increases in HDL.

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