Exercise Training Does Not Reduce Hyperlipidemia in Pigs Fed a High-Fat Diet

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The pig is often used as a model for studying lipoprotein metabolism as it relates to human atherosclerosis, but few studies have examined the complete lipoprotein profile and related enzymes in swine ingesting an atherogenic diet. We examined whether exercise training would moderate the effects of an atherogenic diet on lipoproteins and lipoprotein lipase (LPL) activity in miniature swine. Male (n = 30) and female (n = 32) swine were initially divided into 2 dietary groups: one consumed low-fat (8%) pig chow, and one consumed pig chow supplemented with 2% cholesterol, 17.1% coconut oil, 2.3% corn oil, and .7% sodium cholate (46% kcal from fat). Following 30 days on the diets, pigs from each diet group were further divided into sedentary and exercise trained subgroups, each cell with 6 to 8 pigs. Training occurred 5 days per week on a treadmill in which the intensity and duration were progressively increased during the 16- to 20-week training period to 75 minutes of aerobic running per session. A 4-way analysis of variance (ANOVA) with repeated measures on time indicated that at the conclusion of the study the atherogenic diet caused significantly ($P < .05$) increased cholesterol, triglyceride (TG), high-density lipoprotein cholesterol (HDL-C) and subfractions, low-density lipoprotein cholesterol (LDL-C) and subfractions, and LPL activity in both genders. For cholesterol, TG, HDL-C, HDL_2-C, LDL-C, $LDL_{1\&2}$-C, and hepatic lipase, the female response to the diet was exaggerated compared to the male response. Exercise training produced no group differences or interactions on any lipoprotein variable. These results suggest that an atherogenic diet has a greater impact on the lipoproteins of female miniature swine than males. Furthermore, under the conditions of this study, exercise training does not moderate the effects of an atherogenic diet on lipoproteins.

IN HUMANS, a higher risk for atherosclerosis has been found with increased concentrations of total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) and decreased concentrations of high-density lipoprotein cholesterol (HDL-C) and the subfraction HDL_2-C.[1-3] Recently, evidence has been accumulating that LDL size is an important risk factor for coronary heart disease (CHD), with small, dense LDL strongly associated with CHD.[4,5]

Lipoprotein lipase (LPL) is an enzyme involved in the breakdown of triglyceride (TG)-laden lipoproteins and thus helps clear TG from the plasma. Low LPL activity has been associated with ischemic heart disease as measured by angina pectoris,[6] and certain variations in LPL genes have been correlated with increased susceptibility to CHD.[7]

A high-fat diet can exaggerate the risk of CHD by affecting the lipoprotein profile and associated enzymes.[8] On the other hand, both a session of exercise and a program of exercise training consistently have been shown to alter lipoproteins and associated enzymes in favor of a "cardioprotective" effect.[9] For example, endurance training was reported to increase HDL-C and decrease LDL-C concentrations in men with low HDL-C values.[10]

The pig has many anatomic and physiologic similarities to humans, especially in the cardiovascular system, and thus has been used as a model to study lipoprotein changes with exercise.[8,11,12] Compared to humans, swine typically have lower lipid and lipoprotein values, but feeding a high-fat diet to swine produces lipoprotein concentrations somewhat similar to that of humans on a high-fat diet.[13] Although swine do not have the enzyme cholesterol ester transfer protein (CETP), transfer of cholesterol among lipoproteins still occurs.[13]

Previously, we observed that exercise training had no effect on the lipoprotein profile of pigs eating a normal chow diet.[14] Lipoprotein results from studies in which training was administered to pigs on a high-fat diet are conflicting, with reports showing increased lipoproteins[12] or no changes.[8,15] Stucchi et al[11] used only one diet of 30% fat, but the cholesterol values in these pigs only achieved concentrations of approximately 100 mg/dL after 2 years on the diet. We hypothesized that if pigs were fed a higher fat diet producing cholesterol values as high or higher than those in human CHD, the effects of exercise training would be magnified. In addition, none of the previous studies that used an atherogenic diet and exercise training reported the entire lipoprotein profile, including HDL-C and LDL-C subfractions or LPL activity, variables which may play significant roles in mediating the cardioprotective effect of exercise training.

Therefore, the purpose of this study was to examine the potential for exercise training to moderate the impact of an atherogenic diet on lipoproteins and LPL activity in male and female swine. Based on pilot observations, we hypothesized that exercise training would attenuate the detrimental effect of an atherogenic diet, and the effect would be greater in females than males, since others have observed that female swine have an exaggerated response to a high-fat diet.[16]

MATERIALS AND METHODS

Design

Yucatan male (n = 30) and female (n = 32) miniature swine (Sinclair Research Farm, Columbia, MO) were used. The study was approved and conducted in conformance with the University of Mis-

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souri Animal Care and Use Committee's (ACUC) guidelines on animal research.

All swine were approximately 6 months of age when the study began. The male swine were initially divided into 2 dietary groups; one group consuming a normal (N) pig chow diet (n = 14) and the other consuming a high-fat (HF) pig chow diet (n = 16). Female swine were similarly divided into the N diet group (n = 16) and HF diet group (n = 16). After 4 weeks on the N or HF diet, male and female swine were then randomly divided further into 2 groups, which were sedentary (SED) (16 females, 16 males) and exercise-trained (EXTR) (16 females, 14 males). For the first 4 weeks, pigs were housed together in groups of 8. For the final 16 to 20 weeks, size-matched pairs composed of 1 SED and 1 EXTR pig were housed in stainless steel cages with Tenderfoot flooring (Tandem Products, Minneapolis, MN). An EXTR pig was fed immediately after training along with the matched SED pig. The facility was maintained on a 12-hour light-dark cycle at a controlled temperature of 68 to 72°F.

The effectiveness of the training program was determined by comparing the exercise duration on a treadmill performance test in which speed and grade were incrementally increased until exhaustion as previously described.[17] Heart weight to body weight ratio also was assessed as a measure of heart hypertrophy. In addition, the activity of citrate synthase, a rate-limiting enzyme of the Krebs cycle, was measured in the deltoid muscle according to Srere.[18]

Diets

During the first 30 days of the study, the pigs consumed the diet of their respective group (N or HF) without exercise. For the final 16 to 20 weeks, the pigs continued to consume the same diet and the EXTR pigs participated in the exercise-training protocol.

The pig chow for the N diet consisted of Purina Lab (St Louis, MO) Mini-Pig Diet Breeder pig chow. By weight, this pig chow contained 16.7% protein, 2.6% fat, and 53.2% total carbohydrate and supplied 3.0 kcal $\cdot$ g^{-1} feed (22% of kcal from protein, 8% from fat, and 70% from carbohydrate). The pigs were fed an average of 15 to 20 g/kg once each day for the duration of the study.

The pig chow for the HF diet consisted of Purina Lab Mini-Pig Diet Breeder pig chow supplemented with (% = g $\cdot$ 100 g^{-1} by weight) 2.0% cholesterol, 17.1% coconut oil, 2.3% corn oil, and 0.7% sodium cholate. By weight, this pig chow contained 13% protein, 21.3% fat, and 41.3% total carbohydrate and supplied 4.09 kcal $\cdot$ g^{-1} feed (13% of kcal from protein, 46% from fat, and 41% from carbohydrate). The pigs were fed an average of 15 to 20 g HF feed/kg once each day for the duration of the study. Food intake was adjusted to maintain a stable body weight for both SED and EXTR groups so that the EXTR received 2 to 4 g/kg more feed each day. Water was given ad libitum.

Blood Sampling

Each pig had a baseline blood sample collected. The next sample was taken after consuming either the N or HF diet for 30 days. A final blood sample was collected when the pigs were killed after 16 to 20 weeks of diet or diet plus training. The training duration varied since the pigs were generally in groups of 8, with 2 pigs killed per week. Because of technical considerations for vascular variables collected on the pigs, fasting time was 24 to 32 hours prior to baseline and 30-day samples and 8 to 10 hours prior to the 24-week samples. This last sample was obtained 10 to 12 hours after the last exercise session. Blood was collected by syringe from the jugular vein into a vacutainer containing EDTA. Sodium heparin (100 IU $\cdot$ kg^{-1}) was injected intravenously and after 15 minutes, a second blood sample was collected to measure LPL and hepatic lipase (HL) activities. Samples were centrifuged at 2,000 $\times$ *g* for 15 minutes at 4°C. Plasma was stored immediately at -70°C until analyzed.

Training Protocol

The training program has been described previously.[17] In brief, each animal progressed to running on a motor-driven treadmill for 15 minutes at 6.5 to 7.0 mph plus 60 minutes at 4.0 to 5.0 mph 5 days per week for 16 to 20 weeks.

Plasma Analyses

For all assays below, the 3 samples from an EXTR pig were run with the 3 samples from a SED pig. Cholesterol was analyzed enzymatically using a Sigma Diagnostic kit (Infinity, Procedure #402, St Louis, MO) and quantitated on a spectrophotometer Beckman DU-530 (Fullerton, CA) at 500 nm. The average intra-assay coefficient of variation (CV) was 1.8 %.

TG concentration was assessed enzymatically using a Sigma Diagnostic kit (INFINITY Triglycerides Reagent, Procedure #344, St Louis, MO 63145) and quantitated spectrophotometrically (Beckman model DU-530) at 520 nm. The average intra-assay CV was 2.7%.

Plasma concentrations of total HDL-C, HDL_2-C, and HDL_3-C were measured using a modified heparin-$MnCl_2$-dextran sulfate method[19] with cholesterol for total HDL-C and HDL_3-C assayed as described above. The average intra-assay CV was 0.8%, 1.5%, and 2.3% for HDL-C, HDL_2-C, and HDL_3-C, respectively.

LDL subfractions were isolated by density gradient ultracentrifugation as previously described.[20] Plasma (2.5 mL adjusted to 1.10 g/mL with solid NaBr) was placed in the bottom of the centrifuge tube. This was underlayered with a 0.5 mL volume of 1.3 g/mL NaBr solution to give the sample a flat bottom. The plasma was then overlayered with 1.5 mL of 1.063 g/mL, 3.0 mL of 1.030 g/mL, 3.0 mL of 1.019 g/mL, and 1.0 mL of 1.006 g/mL. The tube thus constituted was spun in an SW41 rotor at 37,000 rpm for 19.5 hours at 20°C. The separate lipoprotein fractions were recovered by puncturing the bottom of the tube (Hoefer Scientific Instruments, San Francisco, CA) and pumping the contents out with a peristaltic pump. Specific volumes were collected with a computerized fraction collection system. The density regions included in LDL_{1-3} subfractions were 1.022 to 1.031, 1.032 to 1.047, 1.048 to 1.063 g/mL, respectively. The LDL subfractions were analyzed for cholesterol as described above and adjusted back to original plasma concentrations. Average CVs for LDL subfractions were as follows: LDL_1-C = 4.8%, LDL_2-C = 3.8%, and LDL_3-C = 2.8%.

LPL activity was determined by the rate at which the enzyme catabolizes TG into free fatty acid (FFA).[21] In brief, postheparin plasma was incubated with [^{14}C] triolein and heat-inactivated serum (a source of apolipoprotein C-II). After incubation with agitation, the reaction was stopped by the addition of an organic mixture (methanol/chloroform/heptane), and a sodium hydroxide solution was used to isolate the liberated FFA.[22] Centrifugation was used to separate the mixture into an upper phase that contained the liberated FFA and a lower phase that contained the TG and partial glycerides. The upper phase was removed and FFA was measured in a scintillation counter as total lipase activity. The addition of a sodium chloride solution to the substrate emulsion was used to inhibit LPL and thus allow the measurement of HL activity. LPL activity was calculated as the difference between total and HL activity. The average intra-assay coefficient of variation was 3.0%, 5.7%, and 2.1% for the activities of total lipase, HL, and LPL, respectively.

Statistical Analyses

Independent variables in this study included gender (male or female), diet (N or HF diet), training group (SED or EXTR), and time (baseline, 4 weeks, and 24 weeks). Statistical analyses were performed using SPSS version 10.0 (SPSS Inc, Chicago, IL) using a 4-factor analysis of variance (ANOVA) with repeated measures on time. Significant *F*

ratios ($P < .05$) were followed with post hoc contrast comparisons. Values are reported as means ± SEM.

RESULTS

Body Weight and Training

All pigs increased in weight from baseline (34.6 ± 0.7 kg) to death (39.5 ± 0.8), with those on HF diet (41.9 ± 1.0) increasing more than those on the N diet (37.1 ± 0.9). Female swine (40.8 ± 1.1 kg) had significantly higher body weight at death than did male swine (38.1 ± 1.0).

There was no significant difference in body weight over time between SED (baseline, 35.6 ± 1.0 kg; 4 weeks, 40.5 ± 1.1; 24 weeks, 38.0 ± 0.8) and EXTR (baseline, 33.7 ± 0.9; 4 weeks, 38.4 ± 1.1; 24 weeks, 36.1 ± 0.8).

The training program used in this study was effective in causing modification in parameters often used as markers of aerobic training (Table 1).

Diet

The HF diet increased all lipoproteins and enzymes, except HL activity, by 4 weeks (Figs 1 through 4). Variables that changed significantly from the 4 weeks to the 24-week sample were TG (Fig 1), HDL-C, and HDL_3-C (Fig 2), which decreased, and HDL_2-C (Fig 2), which increased. As expected, there was a time × diet interaction for all variables (except HL activity), indicating that the response to the HF diet was greater than the N diet over the experimental period.

Gender

There was a main effect for gender for all variables, except for HDL-C and subfractions, indicating that female values were different from male values (Figs 1 through 4). For the lipoproteins, these differences were in the opposite direction from differences reported between women and men. (See Discussion.) For cholesterol (Fig 1), TG (Fig 1), HDL-C, HDL_2-C (Fig 2), LDL-C, and $LDL_{1\&2}$-C (Fig 3), there was a gender × diet interaction, indicating that the female response to the diet was more exaggerated than the male response.

Training

The exercise training program had no significant effect on any of the dependent variables (Tables 2 through 5). Nor were there any significant interactions for training; most importantly, there was no training × diet interaction, which indicated that the training program did not attenuate the effects of the HF diet on lipoproteins (Tables 2 through 5).

Table 1. Markers of Training Effects

Gender	Group	Citrate Synthase Deltoid (μmol/L/min/g)	HW/BW (g/kg)	Endurance Time (min)
Male	SED	15.6 ± 1.8	4.8 ± 0.2	22.4 ± 1.3
	EXTR	21.6 ± 1.5*	5.7 ± 0.2*	32.0 ± 1.1*
Female	SED	12.6 ± 0.6	4.0 ± 0.1	20.3 ± 1.1
	EXTR	18.7 ± 1.6*	5.3 ± 0.1*	34.1 ± 1.5*

NOTE. Values are means ± SE, assessed after 16 to 20 weeks of treatment. For each group n = 16, except male EXTR, n = 14.

Abbreviations: HW, heart weight; BW, body weight. Significant difference, SED *v* EXTR ($P < .05$), by dependent *t* tests.

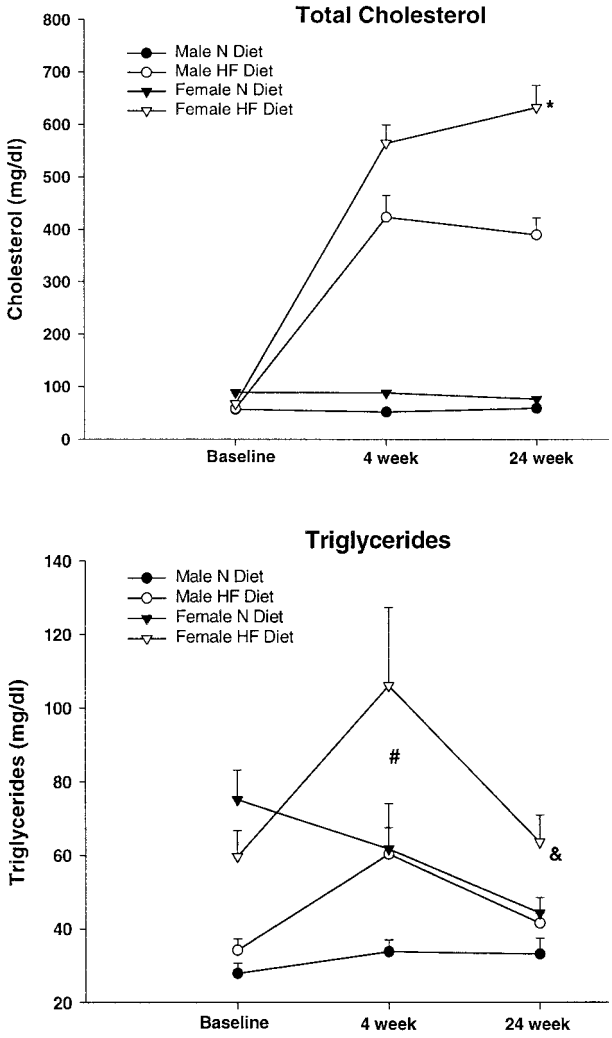


Fig 1. Cholesterol and TG concentrations on HF and N diets with training groups pooled. Values are means and SE. Subgroup numbers are: male N diet = 14, male HF diet = 16, female N diet = 16, female HF diet = 16. The increases in HF diet were significantly greater than N diet, $P < .05$. *Female response to diet was significantly greater than male response, $P < .05$. &Female combined values were significantly greater than male combined values, $P < .05$. #Combined 4-week value was significantly greater than 20 weeks, $P < .05$.

DISCUSSION

Methodology

The final sample was collected only 12 hours following the last exercise session for the EXTR pigs. In humans, a session of exercise may have an effect on the lipoprotein profile during the 24 to 48 hours of recovery.[23] Thus, the timing of sampling during recovery from the last exercise bout of a training program may influence the interpretation of the training effect. However, no data on this confounding effect has been reported in pigs. If the pig response is similar to humans, then the acute

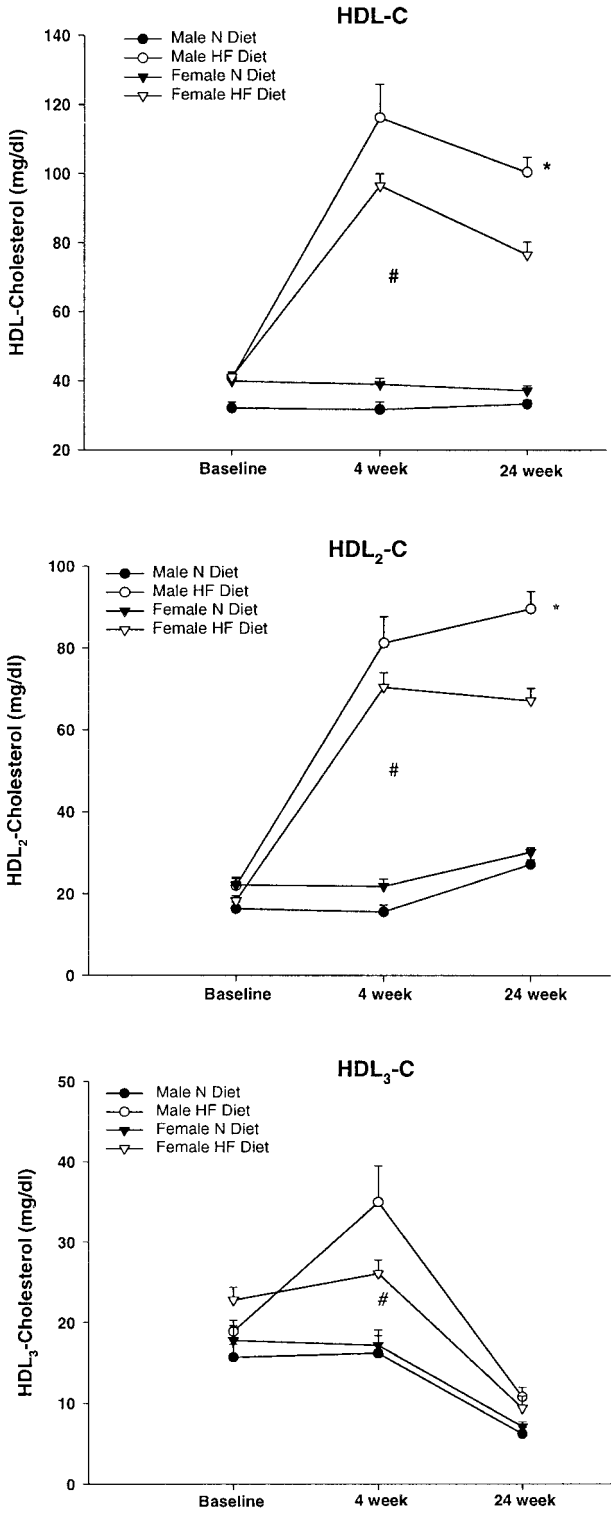


Fig 2. HDL-C and subfraction concentrations on HF and N diets with training groups pooled. Values are means and SE. Subgroup numbers are: male N diet = 14, male HF diet = 16, female N diet = 16, female HF diet = 16. The increases in HF diet were significantly greater than N diet for each variable, $P < .05$. *Female response to diet was significantly lower than male response, $P < .05$. #Combined 4-week value was significantly higher than 24-week value for HDL-C and HDL_2-C and significantly lower for HDL_3-C, $P < .05$.

effect of an exercise session would be expected to cause a decrease in most lipids/lipoproteins, while HDL-C may increase in recovery, even when corrected for plasma volume changes.[23] This would bias the results in favor of a training effect in the EXTR group. Even with this potential bias in favor of an effect, exercise training had no impact on any of the lipoproteins. Therefore, it is doubtful if the timing of the last exercise bout had an impact on the interpretation of the training results.

Diet

As expected, the HF diet administered in this study had a dramatic effect on the lipoprotein profile and LPL activity. These changes are in agreement with other investigators who reported large increases in lipids as a result of a high fat diet in swine. For example, Pedersoli[15] observed that miniature male and female pigs had increased cholesterol and TG concentrations as a result of high fat feeding. Van Oort et al[8] reported that male miniature swine had increased cholesterol, LDL-C, and HDL-C concentrations following a period of high-fat feeding. The increased LPL activity observed with fat feeding in the present study is a novel finding, although Groot et al[24] observed higher LPL activity in piglets fed a lard diet versus those fed a fish oil diet. This increase in LPL activity with fat feeding also has been shown in humans; Campos et al[25] reported that a 46% fat diet fed to men for 6 weeks caused a significant increase in all lipoproteins. The high-fat diet was associated with a 20% increase in LPL activity, compared to the 45% increase in pigs on the HF diet in the present study. Data from other investigations[26,27] demonstrated that adipose tissue LPL activity was increased and muscle LPL activity was decreased with feeding. These results suggest that in the present study the elevated LPL activity observed in postheparin plasma in pigs on the HF diet likely was due to increased enzyme activity in adipose tissue rather than skeletal muscle.

On the other hand, in the present study, HL activity was not significantly affected by the HF diet. Campos et al[25] reported that in humans fed a high-fat diet for 6 weeks, HL activity was increased by a modest but significant 8%. The activities of the lipase enzymes may impact LDL density. Results from other studies indicated that HL activity was correlated to LDL density in male cardiac patients[28] and healthy women.[29] In contrast, Campos et al[25] suggested that the diet-induced increase in LPL activity may have been responsible for the parallel increase in large, buoyant LDL_1. We also observed an increase in the more buoyant LDL subfractions in pigs fed the HF diet. However, Campos et al[25] observed significant decreases in the denser LDL_3 and LDL_4 subfractions, which suggests some potential "cardioprotection" from the high-fat diet, although there was only a 2% net increase in LDL size. In contrast, the denser LDL_3-C subfraction was increased in our pigs fed the HF diet. It is possible that CETP, an enzyme that is found in humans and not pigs[30] and known to be involved in lipoprotein exchange, may be related to these differences in results between pigs and humans. Regardless, in our pigs, the increase in LDL_1-C was much greater than the increase in LDL_3-C (Table 3). We currently are examining the relationship between the change to a more buoyant LDL profile and CHD risk in animals on the HF diet.

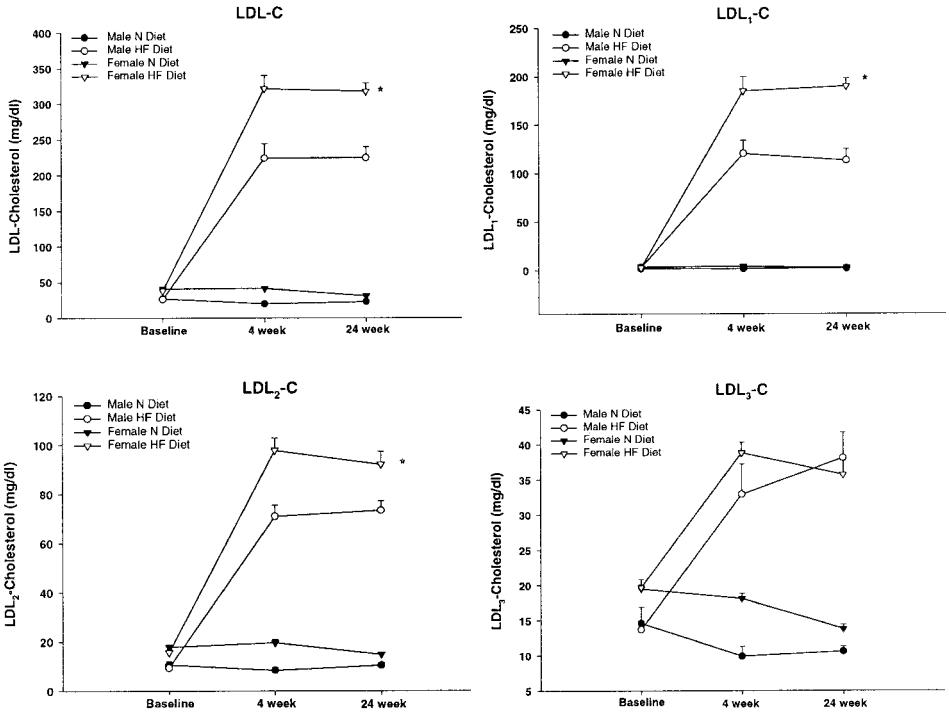


Fig 3. LDL-C and subfraction concentrations on HF and N diets with training groups pooled. Values are means and SE. Subgroup numbers are: male N diet = 14, male HF diet = 16, female N diet = 16, female HF diet = 16. The increase in HF diet was significantly greater than N diet for each variable, $P < .05$. *Female response to diet was significantly greater than male response, $P < .05$.

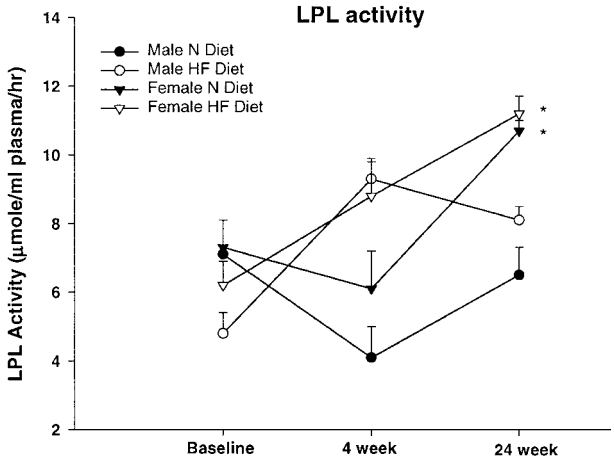
Training

Surprisingly, 16 to 20 weeks of vigorous aerobic exercise training had no impact on the lipoprotein profiles in pigs on a low-fat or high-fat diet. These results confirm our results from miniature swine on regular pig chow (8% fat), which exhibited no lipoprotein impact from 16 weeks of training.[14] However, pigs on this chow diet had very low lipids and thus the training protocol might be expected to have minimal effect. We hypothesized that if the pigs were fed a more atherogenic diet, and thus had less healthy lipoprotein concentrations, that training would be more effective. This was not the case as there were no main effects or interaction effects for training on any variable. Other investigators who have fed pigs a high-fat diet also have reported this puzzling result. For example, Pedersoli[15] observed that male and female miniature swine on a training program for 7 months exhibited no blunting of the lipoprotein concentrations observed in sedentary pigs on a high-fat diet. One limitation of that study was the very short exercise sessions of 10 minutes, which may not have been adequate to induce changes in the lipoproteins. Forsythe et al[31] observed a reduction in cholesterol but no change in HDL-C concentrations in pigs fed a high-fat diet and exercised for only 20 minutes on alternate days for 10 weeks. However, others have confirmed the absence of a training effect on lipoproteins using longer, more aerobic training sessions.[8,12]

On the other hand, Stucchi et al[11] fed female miniature swine a 30% fat diet for 2 years. Those animals on an aerobic training program increased HDL_2-C and LPL activity versus sedentary animals. Training adaptations for cholesterol, TG, and HDL-C were not significant. While the aerobic exercise sessions were shorter (45 minutes) than the training in the present study (75 minutes), the longer duration of the training may account for the positive effects on HDL_2-C and LPL activity. In addition, the fat component of the diet was less severe in the study by Stucchi et al[11] than the diet in previous high-fat diet studies[8,12,15,31] and the present study. This more moderate-fat diet may provide a more appropriate model for examining the effects of exercise training on lipoproteins. This premise is supported by a number of human research studies in which exercise training was effective in altering lipoprotein values in individuals eating an uncontrolled "normal" American diet, which is generally 30% to 35% fat.[9]

The lack of an exercise training effect on plasma lipids in our study and others may be due to the lack of change in body weight. Data from training studies in humans suggest that weight loss may magnify the effects of training on lipoproteins, but weight loss is not a requisite for exercise-induced lipoprotein changes.[9] Based on human studies, the maintenance of body weight in the present study should not have precluded lipoprotein changes.

The lack of a significant effect of training on LPL activity was surprising because other investigators have reported that acute and chronic exercise increased muscle LPL in humans[32,33] and postheparin LPL activity in humans[34] and swine.[11] As illustrated in Fig 4, the HF diet caused a large increase in LPL activity which may have masked any training induced increase. Simsolo et al[35] observed that training was associated with low adipose/muscle LPL ratio compared to when training was withdrawn. In the EXTR pigs, we expected the increased postheparin plasma to represent the summation of the increased muscle LPL activity induced by training plus the increased adipose LPL associated with feeding.[26,27] We previously observed an additive effect of a single exercise session and fat meal on postheparin LPL activity in humans.[36] How-



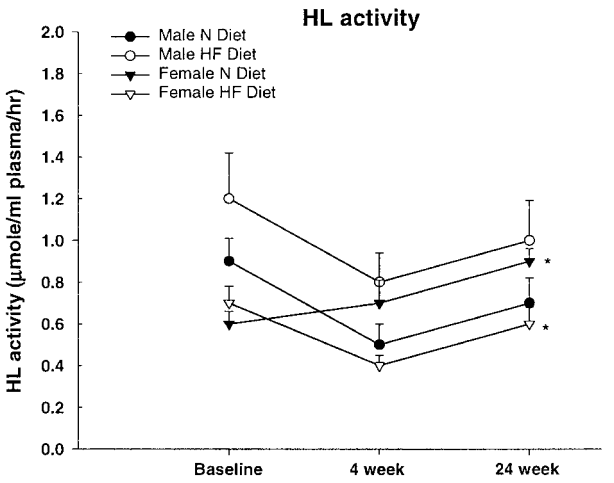


Fig 4. LPL and HL activity on HF and N diets with training groups pooled. Values are means and SE. Subgroup numbers are: male N diet = 14, male HF diet = 16, female N diet = 16, female HF diet = 16. For LPL activity, the increases in HF diet were significantly greater than N diet, $P < .05$. *For LPL activty, combined female values were significantly greater than male values, but for HL combined female values were significantly lower than male values, $P < .05$.

ever, in previous studies,[26,27] it was observed that with fat feeding, muscle LPL activity was decreased, which also may help mask any increase in muscle LPL activity that would occur with training.

On the other hand, neither training nor diet caused a significant change in HL activity (Fig 4). These results are in agreement with previous studies in which exercise-trained individuals had similar HL activity as sedentary dividuals.[34,36] Stucchi et al[11] observed that HL activity was increased with 2 years of aerobic training in swine. The discrepancy in results for HL activity could be due to the length of the training program and acute exercise versus training protocols. Regardless, conclusions about the effect of exercise training in swine on HL activity must await further study.

Gender

Data are sparse for comparing the effects of diet and exercise on lipoproteins between male and female swine in the same study. We previously observed that female miniature swine on the normal diet had higher concentrations of cholesterol, HDL-C, LDL-C, and LDL subfractions regardless of training status.[14] Likewise, in the present study, there was a main effect for gender for most variables with female pigs exhibiting elevated lipoproteins except HDL-C and subfractions. In addition, a gender × diet interaction indicated that the female swine responded more dramatically to the HF diet than the males for cholesterol, HDL-C, HDL_2-C, LDL-C, LDL_1-C, LDL_2-C, and HL activity.

Differences in responses to diet between male and female miniature swine have been previously reported by Reitman and Mahley[16] who observed that a high-fat diet caused a 6-fold increase in cholesterol concentrations in females but only a 2.5-fold increase in males. In that study, TG concentration was reduced in both genders following the HF diet. In the present study, TG concentrations were slightly but significantly higher in pigs on the HF diet versus N diet, and female TG concentrations were higher overall than male pigs. The reason for this discrepancy between the 2 studies is unclear, but may relate to the higher fat content of our diet. Pedersoli[15] also reported that cholesterol and TG concentrations were higher in female than

Table 2. Cholesterol and Triglyceride Concentrations in Sedentary and Trained Pigs

Gender		Trial	N Diet SED	N Diet EXTR	HF Diet SED	HF Diet EXTR
Male	Chol (mg/dL)	Baseline	60.9 ± 8.2	50.1 ± 7.2	62.8 ± 3.5	53.0 ± 3.7
		4 weeks	56.3 ± 5.8	45.0 ± 5.5	472.0 ± 42.7	374.6 ± 70.4
		24 weeks	58.8 ± 4.0	58.4 ± 2.0	403.5 ± 44.1	376.1 ± 50.3
Female		Baseline	89.0 ± 3.7	88.1 ± 5.9	68.6 ± 8.7	65.7 ± 6.2
		4 weeks	90.8 ± 3.6	85.0 ± 3.8	593.7 ± 55.6	534.6 ± 44.3
		24 weeks	74.9 ± 2.4	76.7 ± 2.8	619.3 ± 45.4	645.5 ± 73.0
Male	TG (mg/dL)	Baseline	28.8 ± 4.6	26.7 ± 3.1	38.3 ± 5.5	30.0 ± 2.7
		4 weeks	33.3 ± 4.6	34.5 ± 4.8	63.6 ± 21.0	56.9 ± 19.4
		24 weeks	29.8 ± 6.3	37.4 ± 5.7	39.9 ± 4.3	43.2 ± 3.4
Female		Baseline	76.9 ± 12.2	73.3 ± 11.5	68.0 ± 13.3	51.3 ± 3.7
		4 weeks	63.0 ± 7.7	60.4 ± 9.3	108.3 ± 24.3	103.9 ± 36.5
		24 weeks	42.0 ± 5.9	46.7 ± 6.2	54.7 ± 7.5	72.5 ± 12.5

NOTE. Values are means ± SE. For each subgroup, n = 8, except male N diet EXTR, n = 6. There were no significant training effects or training by diet or training by gender interactions. Abbreviation: chol, cholesterol.

Table 3. HDL-C and Subfraction Concentrations in Sedentary and Trained Pigs

Gender		Trial	N Diet SED	N Diet EXTR	HF Diet SED	HF Diet EXTR
Male	HDL-C, (mg/dL)	Baseline	32.7 ± 2.7	31.3 ± 2.1	43.2 ± 2.2	38.5 ± 2.7
		4 weeks	34.4 ± 2.7	28.0 ± 3.3	120.4 ± 13.5	111.9 ± 14.7
		24 weeks	31.6 ± 1.4	35.6 ± 1.9	96.1 ± 6.3	104.8 ± 6.2
Female		Baseline	39.2 ± 2.0	40.6 ± 4.6	42.6 ± 2.5	39.6 ± 1.7
		4 weeks	38.1 ± 2.1	39.9 ± 3.1	95.8 ± 4.6	97.3 ± 5.6
		24 weeks	35.6 ± 1.2	38.9 ± 2.6	76.0 ± 3.3	77.0 ± 6.9
Male	HDL_2-C (mg/dL)	Baseline	15.8 ± 2.3	17.1 ± 2.4	22.4 ± 2.7	21.4 ± 2.3
		4 weeks	17.5 ± 2.3	12.8 ± 2.2	81.3 ± 9.6	81.0 ± 9.3
		24 weeks	25.9 ± 1.9	28.7 ± 1.7	87.9 ± 5.8	91.4 ± 6.5
Female		Baseline	22.4 ± 2.6	21.9 ± 2.8	20.2 ± 1.7	16.4 ± 1.6
		4 weeks	22.9 ± 2.4	20.7 ± 2.6	68.6 ± 4.8	72.3 ± 5.5
		24 weeks	30.3 ± 1.2	29.9 ± 2.1	66.1 ± 2.9	68.1 ± 5.6
Male	HDL_3-C (mg/dL)	Baseline	16.9 ± 2.4	14.2 ± 2.3	20.8 ± 2.4	17.1 ± 1.2
		4 weeks	16.9 ± 2.1	15.2 ± 4.5	39.1 ± 6.0	30.9 ± 6.7
		24 weeks	5.7 ± 0.7	6.9 ± 1.7	8.2 ± 1.1	13.4 ± 1.6
Female		Baseline	16.8 ± 2.0	18.8 ± 3.2	22.5 ± 2.0	23.2 ± 2.7
		4 weeks	15.2 ± 1.2	19.2 ± 3.6	27.2 ± 2.7	25.0 ± 2.3
		24 weeks	5.3 ± 0.4	9.0 ± 0.7	9.9 ± 2.7	8.9 ± 1.5

NOTE. Values are means ± SE. For each subgroup, n = 8, except male N diet EXTR, n = 6. There were no significant training effects or training by diet or training by gender interactions.

male swine following 7 months of high-fat feeding. Von Duvillard et al[12] found comparable changes in male and female lipoprotein concentrations following fat feeding, but the fractional catabolic rate for HDL-C esters was lower in male pigs than females.

The few human studies comparing the response of men and women to high-fat feeding have generally shown different gender results than demonstrated in pigs. We have reported previously that trained and sedentary males and females responded similarly to a high-fat feeding for postprandial lipemia and LPL activity, HL activity, and CETP.[36] Unlike the results in the present study, Couillard et al[37] found that middle-aged men had a more atherogenic lipoprotein profile that women, perhaps due to the elevated postprandial TG response observed

Table 4. LDL-C and Subfraction Concentrations in Sedentary and Trained Pigs

Gender		Trial	N Diet SED	N Diet EXTR	HF Diet SED	HF Diet EXTR
Male	LDL-C (mg/dL)	Baseline	32.1 ± 5.1	20.2 ± 4.1	28.3 ± 3.0	23.9 ± 1.0
		4 weeks	23.4 ± 3.7	15.0 ± 2.7	252.6 ± 20.4	195.9 ± 32.6
		24 weeks	24.4 ± 3.1	21.0 ± 1.9	231.6 ± 22.5	217.8 ± 22.2
Female		Baseline	38.8 ± 2.2	42.4 ± 2.4	37.3 ± 2.8	38.5 ± 2.8
		4 weeks	41.9 ± 3.5	40.9 ± 2.3	319.3 ± 27.8	324.1 ± 27.0
		24 weeks	32.4 ± 1.6	29.6 ± 1.0	306.9 ± 19.9	328.5 ± 13.9
Male	LDL_1-C (mg/dL)	Baseline	2.3 ± 0.5	1.2 ± 0.3	3.4 ± 0.8	2.6 ± 0.5
		4 weeks	2.0 ± 0.3	1.0 ± 0.3	145.3 ± 16.8	95.4 ± 18.3
		24 weeks	2.3 ± 0.6	1.5 ± 0.6	111.5 ± 15.9	115.0 ± 18.4
Female		Baseline	3.0 ± 0.4	3.5 ± 0.5	2.4 ± 0.4	2.8 ± 0.4
		4 weeks	3.9 ± 0.8	3.6 ± 0.5	186.3 ± 22.9	183.6 ± 21.2
		24 weeks	2.6 ± 0.5	2.4 ± 0.3	178.4 ± 12.0	201.5 ± 11.2
Male	LDL_2-C (mg/dL)	Baseline	12.4 ± 1.9	8.3 ± 1.9	9.9 ± 1.5	8.9 ± 0.7
		4 weeks	10.1 ± 1.8	6.0 ± 1.1	73.4 ± 2.4	68.6 ± 9.2
		24 weeks	11.4 ± 1.6	9.0 ± 1.1	80.1 ± 4.7	66.6 ± 5.3
Female		Baseline	17.1 ± 1.2	18.5 ± 1.6	15.8 ± 1.6	15.5 ± 1.9
		4 weeks	20.3 ± 2.2	18.9 ± 1.5	96.1 ± 7.2	99.8 ± 7.3
		24 weeks	15.6 ± 1.1	13.9 ± 0.6	93.8 ± 8.2	90.4 ± 7.1
Male	LDL_3-C (mg/dL)	Baseline	17.5 ± 3.4	10.7 ± 2.0	15.0 ± 1.9	12.4 ± 1.5
		4 weeks	11.3 ± 2.2	8.0 ± 1.5	34.0 ± 4.9	31.9 ± 7.4
		24 weeks	10.8 ± 1.2	10.5 ± 0.8	40.0 ± 5.1	36.1 ± 5.4
Female		Baseline	18.6 ± 0.8	20.4 ± 0.7	19.1 ± 1.6	20.3 ± 1.6
		4 weeks	17.8 ± 1.0	18.4 ± 0.9	36.9 ± 1.6	40.8 ± 2.5
		24 weeks	14.1 ± 0.9	13.4 ± 0.9	34.8 ± 3.5	36.6 ± 2.2

NOTE. Values are means ± SE. For each subgroup, n = 8, except male N diet EXTR, n = 6. There were no significant training effects or training by diet or training by gender interactions.

Table 5. Lipoprotein Lipase and Hepatic Lipase Activities in Sedentary and Trained Pigs

Gender		Trial	N Diet SED	N Diet EXTR	HF Diet SED	HF Diet EXTR
Male	LPL activity (μmol/mL)	Baseline	7.2 ± 1.2	6.9 ± 1.7	5.7 ± 0.8	3.9 ± 0.9
		4 weeks	4.9 ± 1.0	3.0 ± 1.5	8.6 ± 1.1	9.9 ± 0.6
		24 weeks	5.9 ± 1.1	7.2 ± 1.3	7.9 ± 0.7	8.4 ± 0.5
Female		Baseline	7.0 ± 1.4	7.7 ± 1.0	6.3 ± 0.9	6.0 ± 1.2
		4 weeks	6.0 ± 1.8	6.2 ± 1.3	7.4 ± 1.5	10.2 ± 1.1
		24 weeks	10.8 ± 0.5	10.6 ± 0.4	10.5 ± 0.9	11.8 ± 0.4
Male	HL activity (μmol/mL)	Baseline	0.8 ± 0.1	1.0 ± 0.2	1.4 ± 0.4	1.0 ± 0.2
		4 weeks	0.6 ± 0.1	0.4 ± 0.2	0.5 ± 0.2	1.0 ± 0.2
		24 weeks	0.6 ± 0.2	0.7 ± 0.1	0.8 ± 0.2	1.2 ± 0.3
Female		Baseline	0.6 ± 0.1	0.7 ± 0.1	0.8 ± 0.1	0.7 ± 0.1
		4 weeks	0.7 ± 0.2	0.6 ± 0.1	0.3 ± 0.1	0.4 ± 0.1
		24 weeks	1.0 ± 0.1	0.9 ± 0.1	0.6 ± 0.1	0.6 ± 0.1

NOTE. Values are means ± SE. For each subgroup, n = 8, except male N diet EXTR, n = 6. There were no significant training effects or training by diet or training by gender interactions.

in men versus women. These results support the premise that men have higher CHD risk than women prior to menopause.[38]

The greater diet-induced LPL activity observed in female pigs is the one change that may favor a cardioprotective effect in females versus males. However, the tissue source of the increased LPL activity in female is unknown. It also is unknown if muscle or adipose LPL is associated with a cardioprotective lipoprotein profile. Since trained individuals have lower adipose to muscle LPL ratio,[35] it seems likely that muscle LPL activity is related to decreased CHD risk.

This investigation is the only report in the literature to describe the interaction of an atherogenic diet and exercise training on affecting the comprehensive lipoprotein profile, including HDL-C and LDL-C subfractions or LPL and HL activities, variables which are important markers for the role of diet and exercise in CHD. In addition, we used a high exercise volume (75 minutes, 5 days per week) over a long duration (16 to 20 weeks). Unlike most previous studies, the efficacy of the training was confirmed with standard indicators of aerobic fitness. However, the rigorous exercise program used in the present investigation did not produce changes in the study variables. Data from human studies suggest that lipoproteins in individuals on a typical American diet can be altered by less vigorous training programs than the one used for swine in the present study.[9] In these human studies and in the swine study by Stucchi et al,[11] the fat content of the diets was much lower than in the present study. Thus, one might speculate that the HF diet used in the present study overwhelmed any impact of the vigorous exercise training program.

In conclusion, the results of this study suggest that the lipoprotein response to a high-fat diet is greater in female swine than male. Furthermore, exercise training does not attenuate the atherogenic lipoprotein profile induced by a high-fat diet in male or female swine. Conclusions about whether the more atherogenic lipoprotein profile of female swine is associated with increased CHD must await further research.

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