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Over-the-counter fish oil use in a county hospital: Medication use evaluation and efficacy analysis

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Abstract

BACKGROUND—Little is known about the use and effectiveness of over-the-counter (OTC) fish oil supplements for triglyceride (TG) lowering.

OBJECTIVES—To (1) perform a medication-use evaluation (MUE) and (2) assess the efficacy of OTC fish oil.

METHODS—Retrospective, observational cohort study using electronic medical records and the pharmacy database from Parkland Health and Hospital System in Dallas, Texas. Parkland is a tax-supported county institution that provides patients with single-brand OTC fish oil. Two separate analyses were conducted. Six hundred seventeen patients (prescribed fish oil between July 1, 2012, and August 31, 2012) were included in the MUE analysis and 235 patients (109 fish oil, 72 fenofibrate, and 54 gemfibrozil, prescribed between January 1, 2012, and July 31, 2013) were included in the efficacy analysis. The main outcome measure for the MUE was fish oil prescribing habits including dosages and patient adherence, as defined by medication possession ratio. The main outcome measure for the efficacy analysis was change in lipids measured using the last value before fish oil treatment and the first value after fish oil treatment.

RESULTS—MUE: 617 patients received prescriptions for OTC fish oil. Sixty-four percent were prescribed a total daily dose of 2000 mg. Only 25% of patients were adherent. Efficacy analysis: despite being prescribed suboptimal doses, fish oil reduced TGs by 29% (95% confidence interval, 34.3–22.7). Compared with fish oil therapy, fibrate therapy resulted in a greater TG reduction:

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48.5% (55.1–41.0) with fenofibrate and 49.8% (57.6–40.5) with gemfibrozil ($P < 0001$, both medications compared with fish oil).

CONCLUSIONS—Health care providers prescribe suboptimal doses of fish oil, and adherence is poor. Even at low doses (2 g/d), though, fish oil lowers TGs by 29%.

Keywords

Hypertriglyceridemia; Fish oil; Marine omega-3 fatty acids; Fenofibrate; Gemfibrozil

Introduction

Beginning with studies of Greenland Eskimos, the health benefits of fish oil—specifically the 2 long-chain n-3 polyunsaturated fatty acids eicosapentaenoic acid (EPA, 20:5; n-3) and docosahexaenoic acid (DHA, 22:6; n-3)—have been extensively investigated.¹ The major clinical use of fish oil focuses on its triglyceride (TG)–lowering effect, especially after recent investigations failed to identify a cardioprotective role.^{2–5} DHA and EPA reduce circulating TG levels by as much as 50%, increase high-density lipoprotein cholesterol (HDL-C) by 3%, and raise low-density lipoprotein cholesterol (LDL-C) by 5%.^{6–8}

One third of the United States population suffers from hypertriglyceridemia.⁹ Lifestyle intervention remains the cornerstone of therapy for patients with mild-to-moderate hypertriglyceridemia (TG ranging from 150 to 500 mg/dL), whereas those with higher TG (>500 mg/dL) require pharmacologic intervention, such as fish oil and/or fibrates, to reduce their risk of acute pancreatitis.¹⁰

Many patients take over-the-counter (OTC) fish oil supplements rather than prescription formulations (such as icosapent ethyl; Amarin Pharma Inc, NJ, USA, and omega-3-acid ethyl esters, GlaxoSmithKline, Philadelphia, USA) because of issues with cost and accessibility. Little is known about the use and effectiveness of OTC fish oil supplements for lowering TG levels compared with other commonly used medications such as fibric acid derivatives. Such analyses present a unique challenge because OTC fish oil supplements are sold in a myriad of formulations from several different manufacturers, each of which has different DHA and EPA contents.

The Parkland Health and Hospital System in Dallas, Texas, provides a single OTC brand of fish oil for TG lowering to patients who fill their prescriptions at Parkland pharmacies. Here, we first perform a medication-use evaluation (MUE) for provider prescription practices and patient adherence regarding fish oil. Second, we assess the efficacy and safety of OTC fish oil compared with fibrates.

Methods

We conducted a retrospective, observational cohort study of patients receiving OTC fish oil through the institution's outpatient pharmacies. The Institutional Review Boards at the University of Texas Southwestern Medical Center and the Parkland Office of Research Administration approved the study protocol. Parkland is a tax-supported institution that

primarily serves the indigent population of Dallas County; its pharmacy system dispenses roughly 7000 prescriptions per day.

Parkland pharmacies stock OTC Sea-Omega 50 fish oil in 1000 mg capsules manufactured by Rugby Laboratories (Livonia, MI, USA). Per the product label, each 1000 mg capsule contains 300 mg of EPA and 200 mg of DHA, totaling 500 mg of omega-3 fatty acids per each 1000 mg capsule. The pharmacy stocks fenofibrate in 67 and 200 mg, both strengths manufactured by Global Pharmaceuticals (Philadelphia, PA, USA), and gemfibrozil 600 mg manufactured by Teva Pharmaceuticals (Jerusalem, Israel).

Setting and participants

Two separate analyses, MUE and efficacy analysis, were conducted. The main outcome measure for the MUE was fish oil prescribing habits including dosages and patient adherence, as defined by medication possession ratio (MPR). The main outcome measure for the efficacy analysis was change in lipids measured using the last value before fish oil treatment and the first value after fish oil treatment.

Medication-use evaluation

Using the pharmacy database, we identified all patients who were prescribed fish oil for the first time and filled it at a Parkland pharmacy between July 1, 2012, and August 31, 2012. Medical charts were reviewed through the electronic medical record (EMR) to collect information on lipid panels in the 6 months before initial fish oil prescription and in the 6 months after the date the fish oil prescription was written. Data were collected on fish oil dosage and frequency, and concomitant use of additional TG-lowering medications such as gemfibrozil, fenofibrate, and niacin.

Medication adherence was assessed during the first 6 months from the initial fish oil prescription. Adherence was assessed by calculating the MPR; we used the following formula $MPR = 100 \times ([\text{day supply} \times \text{no. times dispensed}] / 180 \text{ days})$. A patient was considered “adherent” if the MPR was 85% or greater.^{11–13}

Efficacy analysis

We identified patients in the Parkland pharmacy database who were prescribed fenofibrate, gemfibrozil, and fish oil for the first time ever and filled the prescription between January 1, 2012, and July 31, 2013. To assess efficacy of each individual agent as monotherapy, we excluded patients on multiple TG-lowering drugs (eg, combination of fish oil and fenofibrate).

Patients were included in the efficacy analysis if they met the following criteria: 18 years of age, had pretreatment TG ≥ 150 mg/dL, initiated fish oil, fenofibrate, or gemfibrozil between January 1, 2012 and July 31, 2013, had pretreatment and posttreatment fasting lipid panels within 8 months of new prescriptions, and filled all prescriptions at the county institution. Of note, all patients in the Parkland Hospital and Healthcare System are advised to fast before their laboratory draws for lipid panels; however, no documentation is available to confirm fasting status. Exclusion criteria included hemoglobin A1C of $\geq 8.5\%$, fasting

serum glucose of ≥ 200 mg/dL, and thyroid-stimulating hormone of ≥ 5.0 μ IU/mL. We chose to exclude these patients because they have secondary causes of hypertriglyceridemia that can be treated to lower their TGs (eg, insulin for uncontrolled type 2 diabetes),¹⁴ making it difficult to assess the efficacy of fish oil or fibrates. To minimize confounding factors that can potentially impact the efficacy of each individual treatment group, we excluded patients whose lipid-lowering therapies were altered during the study time period.

From the EMR, we collected data on demographic characteristics, vital signs, comorbid conditions, medication profiles, clinical outcomes, therapeutic lifestyle counseling, drug-related adverse events, and laboratory values.

Adherence was measured by calculating MPR with the following formula $MPR = 100 \times (\text{day supply} \times \text{no. times dispensed}) / (\text{days between first fish oil prescription date and the first immediate follow-up TG value date})$. A patient was considered “adherent” if the MPR was 85% or greater.^{11–13}

Statistical analysis

Descriptive statistics were used to describe results from the MUE.

For the efficacy analysis, baseline characteristics were compared among the 3 groups with chi-square tests for categorical variables and Kruskal-Wallis tests for continuous variables. The primary outcome was absolute change in TG levels measured using the last TG value before treatment and the first TG value after treatment. Secondary outcome measures included MPR and change in total cholesterol (TC), LDL-C, and HDL-C. To evaluate the treatment responses of the groups, mixed-effect repeated measures models were used. These models contained a between-group factor (medication), a repeated factor (pretreatment and posttreatment times), and the interaction between group and time. Pairwise comparisons were made with least squares means contrasts derived from the mixed models. Most of the continuous variables were positively skewed and were logged transformed before parametric analyses. However, results are presented in their original units to facilitate interpretation. Continuous variables are presented as mean (standard deviation) or median (interquartile range [IQR]) unless otherwise noted. A 2-sided $P < .05$ was considered statistically significant. Analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). Study data were collected and managed using REDCap electronic data capture tools hosted at UT Southwestern Medical Center.

Results

Medication-use evaluation

Six hundred seventeen patients filled a fish oil prescription at Parkland Health and Hospital System within the specified time frame according to the Parkland pharmacy electronic database. Sixty-four percent of patients were prescribed a total daily dose of 2000 mg and 7% were prescribed total daily doses above 3000 mg of fish oil (Fig. 1). Twenty-five percent of patients were considered adherent. The median baseline TG was 210 mg/dL (range, 45–2469 mg/dL) and HDL was 42 mg/dL (10–87 mg/dL). Eighty percent of patients had lipid panels drawn within 6 months before initiation of fish oil and 57% had follow-up lipid

panels drawn during the following 6 months after fish oil was prescribed. Four percent of patients were concomitantly on gemfibrozil, 8% on fenofibrate, and less than 1% on niacin.

Efficacy analysis

Two hundred thirty-five patients met inclusion criteria (109 receiving fish oil, 72 fenofibrate, and 54 gemfibrozil) in the efficacy analysis. Baseline characteristics are outlined in Table 1. There were significantly more females (55%; $P = .02$) and younger patients (median age, 54 years; $P < .0001$) in the fish oil group. The fish oil group also had significantly more patients with type 2 diabetes (39%; $P = .005$), hypertension (71%; $P = .0001$), and statins use (48%; $P < .0001$). The fenofibrate group had significantly more patients that endorsed alcohol use (51%; $P = .0007$) and smokers (39%, $P = .001$). Patients prescribed gemfibrozil had lower body mass index ($32 \pm 7 \text{ kg/m}^2$ in the fish oil group vs $32 \pm 5 \text{ kg/m}^2$ in the fenofibrate group vs $30 \pm 7 \text{ kg/m}^2$ in the gemfibrozil group; $P = .02$).

There was an overall difference in median TG levels before initiation of medications: 267 mg/dL (IQR, 214–355; $P < .0001$) in the fish oil group, 397 mg/dL (IQR, 282–649; $P < .0001$) in the fenofibrate group, and 527 mg/dL (IQR, 343–731; $P < .0001$) in the gemfibrozil group. The median total daily dose of fenofibrate was 67 mg (range, 67–200 mg), gemfibrozil 1200 mg (1200–1200 mg), and fish oil 2000 mg (1000–6000 mg).

The pretreatment and posttreatment lipid and lipoprotein levels are shown in Figure 2.

Geometric mean (95% confidence interval) percentage changes from pretreatment TG in each group were -28.7% (-34.3 to -22.7 ; $P < .0001$) with fish oil, -48.5% (-55.1 to -41.0 ; $P < .0001$) with fenofibrate, and -49.8% (-57.6 to -40.5 ; $P < .0001$) with gemfibrozil. The median elapsed time between pretreatment and posttreatment lipid panels was 5.1 months (IQR, 3.5–7).

Restricting the analysis to patients adherent to 2 g/d of fish oil, TGs decreased similarly to the total study population (geometric mean, -32.3% [-42 to -21]; $n = 32$). Dividing the 2 g/day fish oil group into quartiles of adherence, we found a nonstatistically significant greater TG reduction in the fourth quartile (most adherent, $n = 20$) vs the first quartile (least adherent, $n = 21$): -28% (-41 to -14) vs -14% (-25.2 to -0.1), $P = .18$.

There were significant differences between treatments in TC reduction (interaction $P = .009$); percent TC changes were median -3.4% (IQR, -16.1 to 4.8) in the fish oil group ($P = .003$), -11.1% (-25.1 to 4.6) in the fenofibrate group ($P < .0001$), and -6.2% (-16.7 to 4.1) in the gemfibrozil group ($P = .1$). In the mixed model analysis, fenofibrate lowered TC more than fish oil ($P = .007$) and gemfibrozil ($P = .008$). There was a significant percentage increase in HDL-C by 5.4% (-4.7 to 17.5) ($P = .005$) in the fish oil group, 13.9% (2.8 to 29.6) in the fenofibrate group ($P < .001$), and 17.7% (-4.0 to 34.0) in the gemfibrozil group ($P < .001$). There were no differences in LDL-C reduction: percent LDL-C changes were 1.4% (-16.8 to 12.5) with fish oil, 6.1% (-27.9 to 22.0) with fenofibrate, and 6.5% (-1.7 to 22.2) with gemfibrozil (omnibus $P = .48$).

Our review of EMR provider notes revealed that patients initiated on gemfibrozil received more therapeutic lifestyle counseling. Fifty percent of patients received dietary advice, including fat and carbohydrate consumption, in the fish oil group, 30% in the fenofibrate group, and 67% in the gemfibrozil group ($P = .0002$). Exercise was recommended for 23%, 17%, and 44%, respectively ($P = .002$), weight loss was suggested for 9%, 7%, and 17%, respectively ($P = .20$), and a nutritionist referral was ordered for 26%, 21%, and 17%, respectively ($P = .47$).

There was a significant increase in mean serum creatinine with fenofibrate (0.1 [0.24], $P < .001$) and gemfibrozil (0.04 [0.10], $P = .04$), whereas no change serum creatinine was observed with fish oil (0.02 [0.16], $P = .83$). There were no follow-up serum creatinine levels in 21% in the fenofibrate group, 26% in the gemfibrozil group, and 15% in the fish oil group within 6 months after initiation of TG-lowering medication.

No significant within-group or between-group changes were noted in body mass index (-0.1 kg/m² with fish oil vs -0.3 kg/m² with fenofibrate vs -0.3 kg/m² with gemfibrozil; interaction $P = .30$), blood pressure (systolic: 1.5 vs 0.03 vs 1.7 kg/m²; $P = .97$; diastolic: -0.4 vs 0.3 vs 2.6 kg/m²; $P = .18$), hemoglobin A1c (0.11 vs -0.14 vs 0.19 kg/m²; $P = .30$), aspartate aminotransferase (0.04 vs $0.3.7$ vs -3.0 kg/m²; $P = .64$), or alanine aminotransferase (-2.3 vs 1.0 vs -1.7 kg/m²; $P = .96$).

Median MPR was 71% (IQR, 39–100) in the fish oil group, 95% (IQR, 63–115) in the fenofibrate group, and 56% (IQR, 32–94) in the gemfibrozil group. Thirty-seven percent of patients were adherent to fish oil, 56% to fenofibrate, and 33% to gemfibrozil. Specifically, 36% patients were adherent to fish oil 2 g/d. Fenofibrate adherence was greater than fish oil ($P = .01$) and gemfibrozil ($P = .02$).

We reviewed EMR provider notes after the initiation of fish oil for any safety issues. Three patients complained of headache shortly after taking fish oil. No patients were discontinued on fish oil due to any side effects.

Discussion

We studied the use of OTC fish oil in a large county hospital system that provides a single-brand supplement and found that most providers prescribe a total daily dose of 2000 mg (400 mg of DHA and 600 mg EPA)—a lower-than-recommended dose for TG lowering—and only 25% of patients adhere to fish oil therapy based on our MUE. In our efficacy analysis, we found that on average fish oil decreased TG by 29% despite most patients taking only 2000 mg/d. Compared with patients who were prescribed fibrates, patients who received fish oil were older, female, had milder hypertriglyceridemia, and more of them had type 2 diabetes and hypertension. Overall, our findings reflect that in clinical practice, providers prescribe lower-than recommended doses of OTC fish oil to patients with mild hypertriglyceridemia and multiple comorbidities.

Our study adds to the current body of knowledge regarding fish oil by reflecting real-world prescribing habits as well as showing efficacy of OTC fish oil. Although randomized controlled trials have shown fish oil to be similarly or less effective than fibrates at lowering

TGs,^{15,16} few studies use OTC fish oil formulations or study real-world settings. A recent retrospective study of human immunodeficiency virus–infected patients, in the Centers for AIDS Research Network of Integrated Clinical Systems Cohort, analyzed the effects of fish oil with methods similar to ours, extracting data from EMR and pharmacy databases.¹⁷ They reported greater TG lowering with fibrates compared with fish oil: adjusted percentage reduction in TG levels between fenofibrate (n = 80) vs fish oil (n = 76) of 16% ($P = .04$) and between gemfibrozil (n = 46) and fish oil (n = 76) of 19% ($P = .04$). Similar to our findings, patients prescribed fish oil had significantly lower pretreatment TG levels than those prescribed fibrates (366 mg/dL in fish oil vs 467 mg/dL in fenofibrate vs 440 mg/dL in gemfibrozil, $P < .01$), and the average time between pre-TG and post-TG measurements was roughly 5 months. However, their data does not reflect OTC fish oil use because most of their patients took prescription fish oil. Similar to our study, most (61%) of patients were taking 2000 mg or less of fish oil; only 2% had a dose of 4000 mg or greater.

Fish oil's TG-lowering impact depends entirely on the omega-3 content, and therefore, the number of capsules required for a total daily DHA and EPA dose of 2000–3000 mg/d. OTC fish oil supplements vary in concentration from approximately 300 to 1000 mg of DHA + EPA per capsule.¹⁸ A minimum of 6 capsules (3000 mg of DHA + EPA) of the institution's OTC fish oil product was required to provide the recommended DHA and EPA content for TG lowering, and only 2 patients in our efficacy analysis and 206 patients in the MUE analysis received such a dose.

We suspect a lack of education regarding the EPA and DHA content of OTC fish oil. Because the recommended daily dose of prescription fish oil products is 4 capsules per day, providers may be mistakenly prescribing an equivalent number of OTC fish oil capsules. Also, providers may be considering adherence: taking 4 capsules may already pose an adherence issue, so 9 capsules may seem overwhelming.

Most randomized comparative studies use higher total daily doses of omega-3 fatty acids.¹⁵ Yet, our findings resemble the fish oil arms in randomized comparative studies with regards to TG lowering. For example, Koh et al¹⁶ reported a 21% reduction in TG with 2000 mg of omega-3 fatty acids daily.

In real-world practice settings, adherence to medications for prevention of asymptomatic chronic diseases is known to be suboptimal.¹⁹ Although arbitrary, an 80% to 85% threshold is often cited for “good adherence” in adherence studies.^{11–13,20} We chose 85% threshold because there is evidence demonstrating significant improvements in outcomes with higher MPR thresholds.^{21,22} In our study, only 25% of patients in the MUE met this criteria for adherence to fish oil therapy. Jackevicius et al¹² found similar results in a study of elderly patients with and without acute coronary syndrome: 2-year statin adherence rates were only 40.1% in acute coronary syndrome arm, 36.1% for chronic coronary artery disease arm, and 25.4% for primary prevention arm. Studies from the pre-statin era found 1-year adherence rates of only 25% to 85% for lipid-lowering therapies.^{23–27} These studies are not generalizable to our study, specifically regarding patient population and duration of therapy, but the studies do provide a reasonable comparison of adherence in patient populations with hyperlipidemia.

Known adverse reactions of fish oil include a fishy aftertaste, mild gastrointestinal symptoms, and bleeding effects.²⁸ We performed chart reviews to identify any possible adverse reactions to fish oil therapy in our cohort; few such adverse reactions were documented in medical charts.

Fibric acid derivatives—fenofibrate and gemfibrozil—lower TGs by approximately 20% to 50%.^{29–35} Findings from our fenofibrate and gemfibrozil groups demonstrated similar percent reductions in TG. Most patients were prescribed fenofibrate at only 67 mg daily despite the recommendation of 200 mg daily as an initial dose for hypertriglyceridemia in patients with normal renal function.³⁶ We suspect that health care providers mistakenly prescribe low-dose fenofibrate with the intention of uptitrating the dosage if needed. We also identified a small but significant increase in serum creatinine with fenofibrate, a known phenomenon that is reversible.^{37–39} We suspect that less frequently dosed medications lend to higher adherence as illustrated by higher adherence rates in fenofibrate arm compared with gemfibrozil and fish oil.^{40,41}

The major strengths of our study is the ability to assess the efficacy of OTC fish oil in a real-world setting, thanks to a single-brand fish oil that is used by our institution. Other strengths include the diversity of patients and comprehensive clinical data regarding adherence, dosing, safety, concomitant medications, comorbidities, and lifestyle modification counseling. Our findings are generalizable to routine patient care because OTC fish oil is often recommended to patients similar to those we included in our analyses.

The study has inherent limitations, including unmeasured confounders, as with any observational study. Baseline characteristics of fish oil, fenofibrate, and gemfibrozil groups were not matched. We excluded patients with uncontrolled diabetes or hypothyroidism because these patients are often treated with insulin or levothyroxine, which can reduce TGs. In clinical practice, many such patients would receive fish oil therapy until hyperglycemia or hypothyroidism can be addressed. Other limitations are inherent to retrospective analysis: we could not confirm fasting status during pretreatment and posttreatment laboratories; subjective data were collected through clinic visit notes using the EMR system; adverse events or side effects and lifestyle modifications may not always be documented.

In our efficacy analysis, fibrates were superior to fish oil, a finding that may be because of differences in degree of baseline hypertriglyceridemia, patient population, concomitant medications, comorbidities, adherence to therapy, extent of education on lifestyle modification, and dosing. Because of these limitations, a randomized clinical trial would better assess the efficacy and safety of OTC fish oil formulations compared with fibrates for the treatment of hypertriglyceridemia.

In conclusion, among patients in a routine clinical setting, fish oil is prescribed at suboptimal doses for hypertriglyceridemia and adherence is poor. Even at low doses (2000 mg), though, fish oil lowers TGs by 29%.

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Figure 1.
Medication use evaluation: total daily doses of fish oil prescribed by health care providers within the Parkland Hospital & Health System.

Figure 2.

Pretreatment and posttreatment lipid and lipoprotein levels for patients prescribed fish oil, fenofibrate, or gemfibrozil (left). Response for each treatment (right) presented as the percentage change from the pretreatment; geometric mean and 95% confidence interval. Left: * $P < .001$ compared with fish oil. The lower and upper limits of the box indicate the 25th and 75th percentiles, the line within the box depicts the median, and the whiskers (error bars) below and above the box indicate the 10th and 90th percentiles. Right: * $P < .005$ compared with pretreatment; † $P < .05$ compared with fish oil; ‡ $P < .05$ compared with fenofibrate. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Table 1

Baseline characteristics of patients prescribed fish oil, fenofibrate, or gemfibrozil

Characteristic	Fish oil (n = 109)	Fenofibrate (n = 72)	Gemfibrozil (n = 54)	P value
Mean age, y	54 (11)	51 (10)	44 (9)	< .001
Female, %	55	39	34	.02
Ethnicity, n (%)				.10
Hispanic white	66 (61)	38 (53)	38 (70)	
Non-Hispanic white	16 (15)	15 (21)	2 (4)	
Black or African American	14 (13)	13 (18)	7 (13)	
Other	13 (12)	6 (8)	7 (13)	
BMI, kg/m ²	32 (7)	32 (5)	30 (7)	.02
Type 2 diabetes, n (%)	42 (39)	25 (35)	8 (15)	.005
Hypertension, n (%)	77 (71)	35 (49)	21 (39)	.0001
Medications, n (%)				
Metformin	27 (25)	20 (28)	10 (19)	.48
Sulfonylurea	12 (11)	9 (13)	6 (11)	.96
Statin	52 (48)	45 (63)	0 (0)	< .0001
Beta blockers	30 (28)	12 (17)	1 (2)	< .0001
Thiazides	30 (28)	15 (21)	8 (15)	.18
Alcohol use, n (%)	27 (25)	36 (51)	13 (25)	.0007
Smokers, n (%)	16 (15)	28 (39)	13 (25)	.001
Total daily dose, mg (range)	2000 (1000–6000)	67 (67–200)	1200 (1200–1200)	
Systolic blood pressure (mm Hg)	129.7 (15.8)	129.2 (17.2)	126.5 (16.8)	.14
Diastolic blood pressure (mm Hg)	79.6 (11.2)	79.5 (11.2)	77.4 (10.4)	.68
Total cholesterol (mg/dL)	203.3 (47)	225 (74.5)	223.7 (77.5)	.07
Triglycerides (mg/dL)	267 (214–355)	397 (281.5–648.5)	527 (343–731)	< .0001
HDL-C (mg/dL)	39.5 (12.8)	36.2 (11.1)	33.4 (10)	.01
LDL-C (mg/dL)	110.6 (40.7)	100.6 (32.4)	100.9 (32.4)	.34
Hemoglobin A1c (%)	6.4 (0.8)	6.3 (0.8)	6.1 (0.8)	.24
Serum glucose (mg/dL)	110.4 (25.3)	113.6 (27.7)	107.4 (30)	.19
Serum creatinine (mg/dL)	0.96 (0.57)	0.88 (0.30)	0.78 (0.19)	.17
AST (U/L)	26.9 (11.2)	26.4 (13.9)	34.2 (35.1)	.33
ALT (U/L)	33.5 (22.3)	30.3 (16.5)	40.4 (37.2)	.45

ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

Continuous variables are summarized as mean (standard deviation) or median (25th–75th percentiles) unless otherwise specified. *P* values are from the Fisher exact test or Kruskal-Wallis test.