Lower High-Density Lipoprotein Cholesterol Concentration Is Independently Associated with Greater Future Accumulation of Intra-Abdominal Fat

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Background: Both intra-abdominal fat (IAF) and high-density lipoprotein cholesterol (HDL-C) are known to be associated with cardiometabolic health. We evaluated whether the accumulation of computed tomography (CT)-measured IAF over 5 years was related to baseline HDL-C concentration in a prospective cohort study.

Methods: All participants were Japanese-Americans between the ages of 34 and 74 years. Plasma HDL-C concentration and CT measurements of IAF, abdominal subcutaneous fat (SCF), and thigh SCF cross-sectional areas were assessed at baseline and at 5-year follow-up visits.

Results: A total of 397 subjects without diabetes were included. The mean±standard deviation HDL-C concentration was 51.6±13.0 mg/dL in men and 66.0±17.0 mg/dL in women, and the IAF was 91.9±48.4 cm² in men and 63.1±39.5 cm² in women. The baseline plasma concentration of HDL-C was inversely associated with the change in IAF over 5 years using multivariable regression analysis with adjustment for age, sex, family history of diabetes, weight change over 5 years, and baseline measurements of body mass index, IAF, abdominal SCF, abdominal circumference, thigh SCF, and homeostatic model assessment for insulin resistance.

Conclusion: These results demonstrate that HDL-C concentration significantly predicts future accumulation of IAF over 5 years independent of age, sex, insulin sensitivity, and body composition in Japanese-American men and women without diabetes.

Keywords: Intra-abdominal fat; Cholesterol, HDL; Epidemiology; Asian Americans

INTRODUCTION

Body fat distribution is accepted as an important risk factor for developing cardiovascular disease (CVD) in the general population in addition to the overall level of adiposity [1,2]. All body fat is not the same regarding the risk of cardiometabolic condi-

tions. Visceral adipose tissue (intra-abdominal fat [IAF]) has emerged as the most pathogenic fat depot and has been reported to be a potential causal factor in the development of diabetes, hypertension, lower insulin sensitivity, dyslipidemia, coronary heart disease, and metabolic syndrome [3-9]. IAF accumulation can increase the risk of cardiovascular complications more strongly than other fat depots [5,6,10,11].

It has been reported that a higher high-density lipoprotein cholesterol (HDL-C) level can decrease the risk of CVD [12]. A low level of HDL-C was identified as a major risk factor for coronary artery disease (CAD) in the Framingham study. Furthermore, in that cohort study, HDL-C levels showed a stronger association with the incidence of CAD than low-density lipoprotein cholesterol (LDL-C) levels [13,14], leading to the inclusion of HDL-C as a key component of the Framingham risk equation. Subsequently, multiple studies have revealed an inverse correlation between HDL-C and CVD risk in humans [15-18]. Moreover, HDL-C is strongly associated with body composition, with a significant inverse relationship between body fat percentage and HDL-C concentration [19,20]. Further research on overall and regional adiposity demonstrated that HDL-C concentrations were correlated with more types of anthropometric measurements (e.g., body mass index [BMI], waist and hip circumference, waist-to-hip ratio, and body fat percentage) than other lipid parameters [21,22]. In particular, it has been reported that there is a significant and inverse correlation between HDL-C and IAF area in men and women [6,9]. The temporal relationship between fat accumulation and HDL-C, however, is not well understood. While both IAF [5,6,9,11] and HDL-C [15-18] have been found to be inversely correlated in cross-sectional studies, whether low HDL-C predates IAF accumulation has not been previously explored to our knowledge [6,9]. Research investigating this question would require a longitudinal assessment of changes in IAF or HDL following baseline measurements. Therefore, we evaluated whether baseline HDL-C concentration was associated with changes in computed tomography (CT)-measured IAF area over 5 years in the prospective Japanese-American Community Diabetes Study.

METHODS

Study population and design

The study population was composed of second- (*Nisei*) and third-generation (*Sansei*) Japanese-Americans of 100% Japanese ancestry (men and women) enrolled in the Japanese-American Community Diabetes Study. We have previously published

a detailed characterization regarding the selection and recruitment criteria of this study population [23,24]. The original cohort sample size of 658 was determined based on the goal of estimating type 2 diabetes prevalence and incidence and not for testing the hypothesis described in this paper. Among the 658 subjects of the original cohort, we excluded 113 subjects who did not complete follow-up examinations or CT scans at baseline or 5-year follow-up. Moreover, 148 subjects were excluded from this study because they had fasting plasma glucose levels equal to or higher than 126 mg/dL, plasma glucose at 2 hours after a 75-g oral glucose tolerance test $\geq$200 mg/dL, or were treated with oral hypoglycemic agents or insulin at baseline or at a 5-year visit. As a result, this study analyzed 397 subjects without diabetes (207 men and 190 women) between 34 and 75 years old (Supplemental Fig. S1 for the participant flowchart). This protocol was approved by the Human Subjects Review Committee at the University of Washington (Institutional Review Board number 35081). All participants signed written informed consent. All evaluations were performed according to the principles of the Declaration of Helsinki.

Clinical and laboratory examination

All examinations were carried out at the General Clinical Research Center, University of Washington Medical Center. A complete physical examination was conducted and medical history and lifestyle factors (e.g., physical activity, alcohol consumption, and smoking) were evaluated using a standardized survey at baseline. Smoking was categorized into three groups (i.e., current smoking at the time of the examination; past smoking prior to the time of the examination but currently not smoking; and never smoked). We used the Paffenbarger physical activity index questionnaire to estimate physical activity levels (usual kilocalories spent weekly) [25]. Alcohol consumption was measured in grams of alcohol per day [25]. A positive family history of diabetes indicated that any first-degree relative had diabetes. BMI was calculated by dividing body weight (kg) by the height squared (m^2). Waist circumference was measured using a tape measure at the position of the umbilicus, generally located between L4 and L5 [26]. Biochemical indicators were measured as reported previously [27]. All blood samples were collected after participants fasted for 10 hours overnight. The hexokinase method was employed to measure plasma glucose using an autoanalyzer (University of Washington, Department of Laboratory Medicine, Seattle, WA, USA). Plasma insulin was analyzed using a radioimmunoassay (Immunoassay Core, Diabetes Research Center, University of Washington, Seattle,

WA, USA). To analyze insulin sensitivity, this study used the homeostasis model assessment of insulin resistance (HOMA-IR) index, which was calculated from fasting plasma glucose and insulin concentrations: (insulin [IU/mL] multiplied by plasma glucose level [mg/dL])/405 [28]. The modified procedures of the Lipid Research Clinics were used to measure lipid and lipoprotein concentrations (Northwest Lipid Research Laboratory, University of Washington, Seattle, WA, USA). The cross-sectional fat area (cm^2) of visceral IAF and abdominal subcutaneous fat (SCF) were analyzed using single 10-mm CT scan slices at the level of the umbilicus. The point midway between the greater trochanter and the superior margin of the patella was used for CT measurements of thigh fat area. CT scan images were analyzed by density contour software (Standard GE 8800 computer software, General Electric Co, Milwaukee, WI, USA). Fat was identified at the attenuation range of –250 to –50 Hounsfield units [29]. The changes (Δ) in IAF and weight were calculated by subtracting baseline values from the values at 5-year follow-up.

Statistical analyses

Continuous variables are displayed as mean±standard deviation, and categorical variables as numbers or percentages. Differences in continuous variables were assessed using the *t* test with unequal variance or non-parametric tests. The differences in the frequencies of categorical data were compared using the chi-square test. We estimated unadjusted linear regression coefficients between temporal changes in IAF from baseline to 5 years (IAF at 5 years minus baseline IAF; ΔIAF) as the dependent continuous variable, and anthropometric variables, metabolic variables, and body composition measures as independent variables. We conducted bivariable analysis and multiple regression analysis to evaluate the independent relationships between ΔIAF and HDL-C concentration while considering various covariates (e.g., age, sex, BMI, insulin resistance, regional fat depots, family history of diabetes, alcohol consumption, physical activities, and smoking). Possible interactions between sex and HDL-C in connection with ΔIAF were examined by adding first-order interaction terms into the regression model. All statistical analyses were carried out using Stata/MP version 15.1 (StataCorp, College Station, TX, USA). Statistical significance was determined at $P<0.05$ for a two-sided test. The data for this study are not available in a public repository but are potentially available to investigators through contact with the senior author of this paper.

RESULTS

Table 1 shows the clinical and laboratory characteristics of the subjects. This analysis included 397 participants without diabetes (207 [52.14%] men and 190 [47.86%] women); their mean age was 51.12±11.79 years, and their BMI was 24.04±3.15 kg/m^2. The mean concentration of HDL-C in men was lower than that in women, as expected. Conversely, also as expected, the mean IAF was greater in men in women. The 5-year follow-up compared to baseline showed higher mean values for BMI, abdomen circumference, glucose levels, insulin, HOMA-IR, triglycerides, IAF, abdominal SCF, and thigh SCF, while lower mean values were seen for total cholesterol, LDL-C, and HDL-C.

The univariate analysis of characteristics associated with 5-year ΔIAF showed significant positive associations with baseline thigh SCF and change in body weight from baseline to 5 years (Δweight change) and negative associations with age and baseline IAF (Table 2). Sex, family history of diabetes, BMI, alcohol consumption, physical activity, smoking, abdominal SCF, and HDL-C and LDL-C levels were not significantly associated with ΔIAF.

Next, bivariable analyses (Table 3) were performed to examine whether other covariates confounded the relationship between baseline HDL-C concentration and 5-year ΔIAF because univariate analysis revealed that HDL-C and 5-year ΔIAF were not significantly correlated. It was found that HDL-C and 5-year ΔIAF were significantly and negatively correlated when baseline IAF was adjusted. Adjustment for other variables shown in Table 3 did not result in HDL-C becoming a significant predictor of 5-year ΔIAF.

Multivariable analyses were carried out to decide whether HDL-C concentration could predict 5-year ΔIAF independently (Table 4). In the first model (model 1), which included age, sex, family history of diabetes, Δ weight change, and baseline BMI, IAF, abdominal SCF, abdomen circumference, thigh SCF, 2-hour glucose, and HOMA-IR, HDL-C concentration was significantly and inversely related to ΔIAF. Age and Δweight change showed significant positive associations, while baseline IAF showed a significant negative association with ΔIAF. Further adjustment of model 1 for alcohol consumption (model 2), alcohol consumption and physical activity (model 3), and alcohol consumption, physical activity, and smoking (model 4) yielded similar results. Age and Δ weight change showed significant positive associations with ΔIAF, while baseline IAF was negatively associated in every model. In these models, HDL-C and 5-year ΔIAF continued to show a significant and negative

Table 1. Baseline Demographic and Clinical Characteristics of Study Subjects

Characteristic	Total ($n=397$)	Male ($n=207$)	Female ($n=190$)
Baseline			
Age, yr	51.1±11.8	51.1±11.8	51.1±11.8
Family history of diabetes	135 (34.0)	62 (30.0)	73 (38.4)
Body mass index, kg/m^2	24.1±3.2	25.1±2.8	22.9±3.1
Abdominal circumference, cm	85.5±8.6	87.6±7.7	83.3±9.0
Alcohol consumption, g/day	5.2±11.1	8.1±13.7	2.0±5.6
Current smoking	56 (14.1)	32 (15.5)	24 (12.6)
Physical activity, kcal/week	2,751.2±1,941.2	3,034.3±2,196.1	2,421.8±1,535.7
Systolic blood pressure, mm Hg	127.2±17.3	130.4±17.4	123.7±16.5
Diastolic blood pressure, mm Hg	76.2±9.4	78.6±8.9	73.6±9.3
Baseline fasting glucose, mg/dL	92.5±10.1	94.9±10.6	89.7±8.8
Baseline 2-hour OGTT glucose, mg/dL	126.6±29.5	126.5±31.0	126.7±27.9
Fasting plasma insulin, mU/mL	13.4±8.1	12.3±6.7	14.6±9.2
HOMA-IR	3.0±1.7	2.9±1.7	3.2±1.8
Total cholesterol, mg/dL	223.7±41.4	227.2±42.0	219.9±40.4
Triglyceride, mg/dL	134.2±104.0	153.4±113.9	113.4±87.6
LDL-C, mg/dL	139.0±36.6	145.7±38.0	131.7±33.5
HDL-C, mg/dL	58.5±16.7	51.6±13.0	66.0±17.0
Baseline IAF, cm^2	78.3±46.7	91.9±48.4	63.1±39.5
Baseline abdominal SCF, cm^2	156.5±77.3	136.7±66.2	178.5±82.9
Baseline thigh SCF, cm^2	65.0±31.5	46.0±18.2	86.3±29.5
Follow-up at 5 years			
Body mass index, kg/m^2	24.7±3.4	25.4±3.0	23.8±3.6
Abdominal circumference, cm	89.4±47.1	89.3±7.9	89.5±67.9
Baseline fasting glucose, mg/dL	97.0±8.6	97.4±8.8	96.5±8.4
Baseline 2-hour OGTT glucose, mg/dL	138.6±29.0	133.4±28.4	144.2±28.7
Fasting plasma insulin, mU/mL	15.5±9.1	16.7±10.3	14.3±7.4
HOMA-IR	3.8±2.3	4.0±2.6	3.5±2.0
Total cholesterol, mg/dL	212.9±36.0	215.2±34.7	210.4±37.2
Triglyceride, mg/dL	144.4±106.9	152.5±110.0	135.6±103.0
LDL-C, mg/dL	129.7±35.9	136.5±34.8	122.4±35.6
HDL-C, mg/dL	55.0±15.7	49.9±12.9	60.5±16.6
IAF, cm^2	87.6±44.6	98.4±45.1	75.6±41.0
Abdominal SCF, cm^2	174.7±86.7	150.8±71.6	201.4±94.2
Thigh SCF, cm^2	65.8±36.0	43.7±17.5	90.9±35.0

Values are expressed as mean±standard deviation or number (%).
OGTT, oral glucose tolerance test; HOMA-IR, homeostasis model assessment of insulin resistance; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; IAF, intra-abdominal fat; SCF, subcutaneous fat.

relationship. Table 5 shows the results of the multivariable models in Table 4 using Z-transformed covariate data to permit comparisons of strengths of the association with ΔIAF. These results demonstrate that HDL-C had a similar strength of asso-

ciation as age in predicting ΔIAF, with baseline IAF and change in weight over 5 years demonstrating the strongest associations. There were 45 post-menopausal women in our population. We performed an adjustment for menopause in the models in Table

Table 2. Univariate Regression Analysis of Change in IAF from Baseline to 5 Years in Relation to Measurements of Lifestyle, Demographic, Body Fat, and Metabolic Characteristics

Change in IAF from baseline to 5 years	Coefficient	95% CI	P value
Age	–0.46364	–0.69859 to –0.22868	<0.001
Female	4.63139	–1.01088 to 10.27365	0.107
Family history of diabetes	–1.20698	–7.14613 to 4.73217	0.690
Body mass index	–0.78305	–1.65870 to 0.09260	0.080
Alcohol consumption	–0.05434	–0.31142 to 0.20274	0.678
Physical activity	–0.00004	–0.00150 to 0.00141	0.955
Current smoker	–1.52412	–10.10930 to 7.06107	0.727
Baseline IAF	–0.20951	–0.26483 to –0.15419	<0.001
Baseline abdominal SCF	–0.01043	–0.04665 to 0.02580	0.572
Baseline thigh SCF	0.09064	0.00173 to 0.17956	0.046
Change in body weight from baseline to 5 years	4.15054	3.46111 to 4.83997	<0.001
Baseline fasting OGTT BLG	–4.32146	–9.37317 to 0.73025	0.093
Baseline 2-hour OGTT BLG	–0.59917	–2.29298 to 1.09463	0.487
Total cholesterol	–1.53935	–4.20926 to 1.13057	0.258
Triglyceride	–1.12349	–3.53585 to 1.28887	0.360
LDL-C	–1.29330	–4.29901 to 1.71241	0.398
HDL-C	2.64755	–3.90249 to 9.19759	0.427
Baseline fasting insulin	–0.00926	–0.06911 to 0.05058	0.761
HOMA-IR	–0.31140	–1.96898 to 1.34617	0.712

IAF, intra-abdominal fat; CI, confidence interval; SCF, subcutaneous fat; OGTT, oral glucose tolerance test; BLG, blood glucose; LDL-C, low-density lipoprotein cholesterol; HDL-C, high-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance.

4 and obtained nearly identical and statistically significant results for the association between HDL-C and ΔIAF (data not shown).

Since both IAF and HDL-C vary by sex, this study examined the relationship between HDL-C and ΔIAF, which can be affected by sex, by adding a sex×HDL-C interaction term to the multivariable models (Table 4). No significant interaction was found between HDL-C and sex when this term was added (data not shown). Few subjects were taking lipid-lowering medications during the course of this research. The results shown in Table 4 were similar when we repeated models 1–4 after excluding the eight participants taking lipid-lowering medications (data not shown).

DISCUSSION

This study prospectively evaluated Japanese-American men and women without diabetes, finding that HDL-C concentration and future accumulation of IAF were negatively related over 5 years and that this association was independent of age, sex, insulin sensitivity, glycemia, body composition, smoking and lifestyle factors potentially affecting HDL-C levels such as alcohol consumption and physical activity. These results indicate that greater accumulation of IAF occurred in the subjects with lower baseline HDL-C concentrations in this population.

Previous cross-sectional studies have revealed that IAF and HDL-C concentration are related. The inverse relationship between IAF and HDL-C concentration has also been reported in other populations showing a variety of characteristics, including obese, non-obese, dyslipidemic, and non-diabetic subjects [30-34]. A negative relationship between IAF and HDL-C concentration was also reported in a previous cross-sectional study conducted in this Japanese-American cohort [3]. Moreover, it was also reported that regular endurance exercise helped to increase low HDL-C levels with an accompanying decrease in abdominal obesity, demonstrating that changes in HDL-C concentrations are associated with changes in abdominal obesity in response to an intervention [35].

Interestingly, the appearance of an association between HLD-C and ΔIAF depended on adjustment for covariates in the re-

Table 3. Bivariable Analysis of the Prediction of Change in IAF in Relation to Measurements of Lifestyle, Demographic, Body Fat, and Metabolic Characteristics

Model	HDL-C coefficient	P value
HDL-C	2.64755	0.427
HDL-C, Age	2.02412	0.537
HDL-C, Female	0.33474	0.928
HDL-C, Family history	2.58178	0.440
HDL-C, Body mass index	0.22131	0.952
HDL-C, Alcohol	2.81306	0.402
HDL-C, Physical activity	2.66800	0.425
HDL-C, Current smoking	2.73997	0.426
HDL-C, Baseline IAF	−11.34154	0.001
HDL-C, Baseline abdominal SCF	2.46807	0.462
HDL-C, Baseline thigh SCF	1.24987	0.714
HDL-C, Weight change for 5 years	−1.10593	0.702
HDL-C, Fasting glucose	1.34272	0.696
HDL-C, Postprandial glucose	2.53154	0.449
HDL-C, Total cholesterol	2.76191	0.408
HDL-C, Triglyceride	1.58845	0.672
HDL-C, LDL-C	2.29767	0.495
HDL-C, Fasting insulin	2.55711	0.460
HDL-C, HOMA-IR	2.49944	0.473

IAF, intra-abdominal fat; HDL-C, high-density lipoprotein cholesterol; SCF, subcutaneous fat; LDL-C, low-density lipoprotein cholesterol; HOMA-IR, homeostasis model assessment of insulin resistance.

gression analysis. While we consistently observed associations in the same direction between ΔIAF with change in weight and baseline IAF in both unadjusted and adjusted analyses, the relationship between ΔIAF and HDL-C was not observed until baseline IAF was adjusted. It has been reported that body weight changes are related to HDL-C as well as IAF, with an IAF increase associated with an HDL decrease [20]. We observed a negative association between baseline IAF and ΔIAF, such that greater baseline IAF predicted less IAF accumulation over 5 years. Additionally, greater IAF at baseline was related to lower baseline HDL-C. Owing to this strong relationship between baseline IAF and HDL-C, baseline IAF was adjusted to control confounding and permitted identification of the negative relationship between HDL-C and ΔIAF.

There are several possible mechanisms whereby high HDL-C concentration may prevent accumulation of IAF. HDL-C is generally accepted as a friendly scavenger that promotes cholesterol efflux from peripheral cells and transfers the obtained cholester-

ol to the liver for excretion, which constitutes the main reverse cholesterol transport channel [36]. Given this finding, HDL-C might lessen lipid accumulation in adipocytes [37], which could possibly reduce accumulation of IAF. HDL-C contributes to modulating body fat content by directly advancing catecholamine-elicited, but not basal lipolysis, possibly through a receptor-mediated mechanism with apolipoprotein A-I (ApoA-I) [38]. Decreased levels of circulating HDL-C and ApoA-I, its major protein, may contribute directly to causing or maintaining the obese condition [38]. In addition, HDL-C could serve as a marker for metabolic activity. Metabolically healthy obese subjects had 21% higher HDL-C concentrations and a resting metabolic rate per BMI unit that was 25% higher than metabolically unhealthy obese individuals [39].

In addition, human clinical and animal studies have reported that HDL-C has direct impacts on adipocyte metabolism. Serum adiponectin is also positively associated with HDL-C [40]. Moreover, a longitudinal study from our Japanese-American population showed that low plasma adiponectin concentration was a valid independent predictor for abdominal visceral fat accumulation [41]. Finally, higher HDL-C due to ApoA-I transfer influences the gene expression associated with metabolism of fatty acid in adipose tissues and potently decreases triglyceride concentration. Furthermore, HDL-C is positively associated with plasma adiponectin concentration and adiponectin expression in adipocytes *in vivo*.

The importance of this study includes the fact that direct fat measurements were made using CT scans, enabling an accurate assessment of fat depots in the regions of interest and permitting an evaluation of change over time. As far as we are aware, this study is the first effort to examine the relationship between HDL-C and change in IAF. The results of this study imply that HDL-C concentration is a readily available marker for predicting IAF accumulation as well as CVD risk.

Nevertheless, there are several limitations of this study. First, because the subjects in this study were exclusively Japanese-Americans, these results might not be applicable to other ethnic groups. Secondly, the present findings arise from an observational study design, precluding conclusions about causality. Additionally, due to the nature of all observational research, although all known covariates were adjusted, unknowable factors could have caused confounding in the relationship between the concentration of serum HDL-C and adiposity. This study also could not evaluate the functional states of HDL-C or further examine the structure of HDL-C. Finally, physical activity meeting or exceeding a certain level of caloric expenditure should be

Table 4. Multivariable Linear Regression Analysis of the Prediction of Change in IAF in Relation to Measurements of Lifestyle, Demographic, Body Fat, and Metabolic Characteristics

Change in body IAF from baseline to 5 years	Model 1 β	Model 1 P value	Model 2 β	Model 2 P value	Model 3 β	Model 3 P value	Model 4 β	Model 4 P value
HDL-C	−12.6953	<0.001	−13.5757	<0.001	−13.0597	<0.001	−13.2910	<0.001
Age	0.4800	<0.001	0.4877	<0.001	0.4794	<0.001	0.4664	<0.001
Female	−4.5793	0.2900	−3.6519	0.4080	−3.4003	0.4410	−3.1102	0.4820
Family history of diabetes	−0.5470	0.8260	−0.4996	0.8400	−0.3766	0.8790	−0.6020	0.8090
Body mass index	0.5963	0.4120	0.6191	0.3950	0.8393	0.2590	0.8036	0.2840
Baseline IAF	−0.3412	<0.001	−0.3437	<0.001	−0.3494	<0.001	−0.3478	<0.001
Baseline abdominal SCF	0.0177	0.5120	0.0175	0.5150	0.0146	0.5870	0.0144	0.5960
Baseline thigh SCF	0.0390	0.5100	0.0415	0.4840	0.0266	0.6570	0.0292	0.6270
Change in body weight from baseline to 5 years	3.9405	<0.001	3.9427	<0.001	3.9803	<0.001	3.9656	<0.001
Baseline 2-hour OGTT BLG	1.5661	0.0380	1.6152	0.0330	1.5600	0.0390	1.4709	0.0530
HOMA-IR	0.4007	0.6250	0.3709	0.6510	0.2945	0.7200	0.3152	0.7010
Alcohol consumption			0.1177	0.2970	0.1145	0.3100	0.1072	0.3570
Physical activity					−0.0009	0.1600	−0.0009	0.1470
Current smoker							−2.4761	0.5050
R squared		0.4004		0.4022		0.4054		0.4074

IAF, intra-abdominal fat; HDL-C, high-density lipoprotein cholesterol; SCF, subcutaneous fat; OGTT, oral glucose tolerance test; BLG, blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance.

Table 5. Multivariable Linear Regression Analysis of the Prediction of Change in IAF in Relation to Measurements of Lifestyle, Demographic, Body Fat, and Metabolic Characteristics Using Z-Transformed Data for Covariates

Change in body IAF from baseline to 5 years	Model 1 β	Model 1 P value	Model 2 β	Model 2 P value	Model 3 β	Model 3 P value	Model 4 β	Model 4 P value
HDL-C	−5.4478	<0.001	−5.8256	<0.001	−5.6042	<0.001	−5.7035	<0.001
Age	5.6874	<0.001	5.7798	<0.001	5.6814	<0.001	5.5263	<0.001
Female	−4.5793	0.290	−3.6519	0.408	−3.4003	0.441	−3.1102	0.482
Family history of diabetes	−0.5470	0.826	−0.4996	0.840	−0.3766	0.879	−0.6020	0.809
Body mass index	1.9748	0.412	2.0505	0.395	2.7796	0.259	2.6613	0.284
Baseline IAF	−18.3480	<0.001	−18.4851	<0.001	−18.7874	<0.001	−18.7021	<0.001
Baseline abdominal SCF	1.3502	0.512	1.3385	0.515	1.1189	0.587	1.1014	0.596
Baseline thigh SCF	1.2272	0.510	1.3047	0.484	0.8375	0.657	0.9188	0.627
Change in body weight from baseline to 5 years	14.0051	<0.001	14.0129	<0.001	14.1464	<0.001	14.0943	<0.001
Baseline 2-hour OGTT BLG	7.9810	0.038	8.2312	0.033	7.9498	0.039	7.4957	0.053
HOMA-IR	1.3593	0.625	1.2584	0.651	0.9991	0.720	1.0695	0.701
Alcohol consumption			1.4078	0.297	1.3693	0.310	1.2828	0.357
Physical activity					−1.5779	0.160	−1.6483	0.147
Current smoker							−2.4761	0.505
R squared		0.4004		0.4022		0.4054		0.4074

IAF, intra-abdominal fat; HDL-C, high-density lipoprotein cholesterol; SCF, subcutaneous fat; OGTT, oral glucose tolerance test; BLG, blood glucose; HOMA-IR, homeostasis model assessment of insulin resistance.

associated with HDL-C [42]. However, the only measure of physical activity available to us came from a baseline questionnaire that might not have fully reflected participants' energy expenditure during the follow-up period. Despite these limitations, we believe that this is the first prospective study indicating that it may be possible to predict change in IAF measured by imaging using HDL-C.

In conclusion, HDL-C was significantly related to the accumulation of IAF in Japanese-Americans. The findings of this longitudinal analysis present novel evidence supporting the hypothesis that HDL-C or a correlate may contribute to the accumulation of IAF.

CONFLICTS OF INTEREST

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AUTHOR CONTRIBUTIONS

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