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Distribution of 10-Year and Lifetime Predicted Risk for Cardiovascular Disease Prior to Surgery in the Longitudinal Assessment of Bariatric Surgery-2 Study

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Abstract

Primary prevention guidelines recommend calculation of lifetime cardiovascular disease (CVD) predicted risk among individuals who may not meet criteria for high short-term (10-year) ATP-III risk for coronary heart disease (CHD). Both extreme obesity and bariatric surgery are more common among women, who often have low short-term predicted CHD risk. The distribution and correlates of lifetime CVD predicted risk, however, have not yet been evaluated among bariatric surgery candidates. Using established 10-year (ATP-III) CHD and lifetime CVD risk prediction algorithms and pre-surgery risk factors, participants from the Longitudinal Assessment of Bariatric Surgery-2 study without prevalent CVD (n=2070) were stratified into 3 groups: low 10-year (<10%)/low lifetime (<39%) predicted risk, low 10-year (<10%)/high lifetime (≥39%) predicted risk, and high 10-year (≥10% predicted risk or diagnosed diabetes.) Participants were predominantly white (86%), women (80%), with a median age of 45 years and median BMI of 45.6 kg/m². High 10-year CHD predicted risk was common (36.5%), and associated with diabetes, male sex and older age, but not with higher BMI or hs-c-reactive protein. Most (76%) participants with low 10-year predicted risk had high lifetime CVD predicted risk, which was associated with dyslipidemia and hypertension, but not with BMI, waist circumference, HDL cholesterol or hs-C-reactive protein. In conclusion, bariatric surgery candidates without diabetes or existing CVD are likely to have low short-term, but high lifetime CVD predicted risk. Current data support the need

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for long-term monitoring and treatment of elevated CVD risk factors among bariatric surgery patients, to maximize lifetime CVD risk reduction.

Clinical Trial Registration—Long-term Effects of Bariatric Surgery, #NCT00465829, <http://www.clinicaltrials.gov/ct2/results?term=%23NCT00465829>

Keywords

Cardiovascular disease; extreme obesity; bariatric surgery; lipids

Introduction

Recently, long-term, or lifetime cardiovascular disease (CVD) risk scores have been developed, using long-term follow-up data to capture the long incubation period for development of CVD. Using 30 year follow-up data in Framingham participants, Lloyd-Jones et al. calculated that at age 50, the lifetime predicted CVD risk (i.e., risk of CVD during remaining lifetime) is 1 in 2 for men and 1 in 3 for women.¹ Lifetime CVD predicted risk has been stratified into high (>39% risk of a CVD event during lifetime follow-up) vs. low (<39% risk) according to categories of traditional CVD risk factors.¹ Applying this lifetime CVD risk stratification to NHANES 2006 data showed that 2 in 3 US adults with “low” 10-year predicted coronary heart disease (CHD) risk have high lifetime predicted CVD risk.² Primary prevention guidelines recommend the use of long-term, or lifetime, CVD predicted risk stratification¹ in addition to short-term, 10-year (Framingham/ATP-III) CHD risk estimation, particularly among women and younger individuals who are less likely to meet criteria for high 10-year CHD risk.^{3,4} However, although both extreme obesity⁵ and bariatric surgery⁶ are more common among women than men, the distribution and correlates of lifetime predicted CVD risk has not yet been evaluated among bariatric surgery candidates or other individuals with extreme obesity. Therefore, the objective of the current report is to describe the pre-surgery distribution and correlates of lifetime CVD predicted risk as an adjunct to 10-year CHD predicted risk among adults enrolled in a large, multi-center observational study of bariatric surgery.

Methods

As previously described in detail, the Longitudinal Assessment of Bariatric Surgery (LABS) is a series of NIH-funded multi-center longitudinal observational cohort studies designed to rigorously assess the risks and benefits of bariatric surgery.⁷ LABS includes several studies (LABS-1, LABS-2, and LABS-3) including progressively smaller cohorts with more detailed data collection. Between February 1, 2006 and February 17, 2009, patients at least 18 years old without previous weight loss surgery, seeking bariatric surgery by participating surgeons at ten locations throughout the United States were identified for recruitment to LABS-2. The study is registered at www.clinicaltrials.gov, all centers had institutional review board approval, and all participants provided informed consent. By study enrollment closure (April 2009), 2458 participants attended a baseline (pre-surgery) research visit, which occurred after the surgery approval process was complete and within 30 days prior to their scheduled bariatric surgical procedure. Of these, 186 were excluded from the current report due to missing key data points at baseline (i.e., CVD, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), systolic or diastolic blood pressure (SBP or DBP), hypertension medication or smoking), and 202 were excluded for prevalent CVD (defined as history of ischemic heart disease, heart failure or stroke), because they are not part of the lifetime risk scoring algorithm, leaving a sample size of 2070.

Data used in this study were collected at the baseline (pre-surgery) research visit. Age, sex, race, ethnicity, medications, diabetes and cigarette smoking were self-reported via

standardized questionnaire, completed 30 days of surgery, after pre-surgery medical workup. Current smoking was defined as smoking within the last year to avoid bias caused by recent quitting. Height and weight were measured according to standard protocol and body mass index (BMI) was calculated as kg/m^2 .⁷ Waist circumference was measured following a standard protocol using Gulick II Tape Measure (model 67020), measuring around the abdomen horizontally at the midpoint between the highest point of the iliac crest (hip bone) and lowest part of the costal margin (ribs). A single measurement of systolic and diastolic blood pressure was obtained by a trained and certified researcher using a Welch Allyn Spot Vital Signs monitor 4200B. Sleep apnea and hypertension were determined by clinical researchers based on chart-review, physical assessment or self-report (e.g., sleep study or self-reported CPAP use, blood pressure measurements, and medication).

Personnel at the clinical sites drew fasting blood specimens. All assays in this report were performed by the Northwest Lipid Metabolism and Diabetes Research Laboratories (Seattle, WA). Using plasma samples, total cholesterol (TC) and triglycerides (TG) were quantified using a Roche Modular-P autoanalyzer using methods standardized to the Centers for Disease Control and Prevention Reference Methods. High density lipoprotein cholesterol (HDL-C) was determined using precipitation procedures with polyethylene glycol (Immuno, Vienna, Austria) low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation, except for participants whose TG ≥ 400 mg/dl, for whom LDL-C was measured directly via beta-quantification. Non-HDL-C was calculated as TC minus HDL-C. High-sensitivity C-reactive protein (hsCRP) was measured using the Behring Nephelometer II. Lipid levels were reported as continuous variables and using the following cutoffs for non-optimal lipids: TC ≥ 200 mg/dl, LDL-C ≥ 100 mg/dl, Non-HDL-C ≥ 130 mg/dl, TG ≥ 150 mg/dl, and HDL-C < 40 mg/dl for men and HDL-C < 50 mg/dl for women.

Participants (without baseline CVD) were classified into 3 risk strata according to 10-year ATP-III CHD predicted risk,³ and lifetime CVD predicted risk¹: low 10-year/low lifetime, low 10-year/high lifetime and high 10-year predicted risk, as has been reported for NHANES 2006 data.² Specifically, short-term (10-year) predicted risk for hard CHD (myocardial infarction or coronary death) risk was calculated using Framingham point scores via the ATP-III risk assessment tool.³ Points are assigned for sex, age, total cholesterol, HDL-C, SBP, treatment for hypertension, diabetes and cigarette smoking. “High” 10-year predicted CHD risk was defined as 10-year hard CHD risk $\geq 10\%$, or diabetes, and “low” 10-year predicted risk as 10-year hard CHD risk $< 10\%$ and no diabetes.³

For participants with low 10-year CHD predicted risk, lifetime predicted risk for CVD (all atherosclerotic CVD) was calculated using the existing lifetime CVD risk algorithm, with cutpoints for SBP, DBP, TC, diabetes, and smoking, as previously described.¹ “High” lifetime CVD predicted risk was defined as ≥ 1 elevated or major risk factor, i.e., SBP ≥ 140 or DBP ≥ 90 or treated hypertension, or TC ≥ 200 mg/dl or treated hypercholesterolemia, or diabetes, or current cigarette smoking. “Low” lifetime CVD predicted risk was defined as meeting all of these criteria: SBP < 140 mmHg, DBP < 90 mmHg, TC < 200 mg/dl, no diabetes, not currently smoking cigarettes, and no anti-hypertensive or lipid-lowering medications. “High” and “low” lifetime CVD predicted risk have been previously defined,^{2,8} based on lifetime risk estimates from Framingham showing that “high” had 39% lifetime risk and “low” had $< 39\%$ lifetime risk of CVD.¹ This lifetime risk stratification has also been shown to differentiate higher vs. lower levels of subclinical atherosclerosis among younger adults in multi-ethnic cohorts.⁸ In a secondary analysis, lifetime CVD risk strata were reclassified by adding low HDL-C (< 40 mg/dl for men, < 50 mg/dl for women) to the definition of high lifetime risk, as was previously reported using NHANES 2006 data.²

SAS v. 9.2 was used for all analysis. Results are reported as median (interquartile range) or percentage (standard error; SE). Between-group differences were tested using Pearson's chi-square test for differences in proportions or the Wilcoxon-rank sum test. Logistic regression was used to test whether differences in lipid categories by sex or risk strata persisted when adjusted for lipid lowering medication.

Results

Most study participants were white women, with median age of 45 years and median BMI of 45.8 kg/m² (Table 1). Diabetes, hypertension, and sleep apnea were common, and median hsCRP levels were high, but the prevalence of smoking was low. Median lipid levels were not high, but non-optimal lipid levels were common. Compared with study participants, LABS-2 participants excluded from this report because of existing CVD prior to surgery (n=202) had similar median BMI and prevalence of smoking, but were more likely to be men, older, with a higher prevalence of diabetes, hypertension, sleep apnea and use of anti-hypertensive or lipid-lowering medications, but lower median levels of hsCRP and most lipids (Table 1). Among study participants, compared with women, men had higher median BMI and TG levels and were more likely to have diabetes, hypertension, sleep apnea or to use lipid-lowering or anti-hypertensive medication, but had a lower prevalence of non-optimal lipids (except for HDL-C and TG), and lower median hsCRP. In logistic regression models adjusted for lipid-lowering medications, men remained less likely to have non-optimal TC, LDL-C and non-HDL-C (odds ratio (OR) range= 0.59 to 0.76, all p<0.05), whereas the OR(95% confidence interval) for TG ≥ 150 mg/dl was 1.23 (0.99, 1.54), p=0.06 for men vs. women.

Over a third (36.5%) of participants without CVD had high short term (10-year) predicted risk, 48.0% had low 10-year but high lifetime predicted risk, and only 15.5% had both low 10-year and low lifetime predicted risk (Table 2). Therefore, 75.6% (993/1314) of those with low 10-year risk had high lifetime risk. The addition of low HDL-C to the definition of high lifetime risk (Table 2) reclassified 210 participants as high lifetime risk, such that 91.3% (1200/1314) of those with low 10-year CHD predicted risk had high lifetime CVD predicted risk. Low 10-year/high lifetime risk was more common for women vs. men and for younger vs. older men (Figure.) For women in each age group, and for men younger than 50 years, 50% of those with low 10-year risk had high lifetime risk, whereas high 10-year CHD risk predominated for men older than 50 years.

Characteristics of participants in each risk category are shown in Table 3. Diabetes status was the greatest contributor to 10-year risk classification; only 10.6% of the high 10-year CHD risk category did not have diabetes. The majority (92.3%) of individuals with diabetes had other elevated or major risk factors (data not shown). Compared with overall low 10-year risk, high 10-year risk was also characterized by male sex, older age, lower HDL-C, SBP, hypertension and greater use of anti-hypertensive medications, by definition. High 10-year CHD risk was also characterized by a larger waist circumference, higher triglycerides, and more non-optimal triglycerides, sleep apnea, and lipid-lowering medication use (not included in the risk algorithm). High 10-year risk was not characterized by higher BMI, and was associated with lower median DBP, hsCRP, total cholesterol, LDL-C and non- HDL-C.

Most of those with low 10-year predicted risk had high lifetime CVD risk, characterized by a higher prevalence of smoking, hypertension and higher TC (by definition), and older age, higher LDL-C and non-HDL-C (not part of the lifetime risk algorithm). Interestingly, sex, ethnicity, BMI, waist circumference, hsCRP, and HDL-C, also not part of the lifetime risk algorithm, were not statistically different between the low 10-year/low lifetime and low 10-

year/high lifetime groups. Sleep apnea was more common for high vs. low lifetime risk but the difference did not reach statistical significance.

Discussion

This is the first report of the distribution and correlates of long-term (lifetime) predicted CVD risk in conjunction with short-term (10-year) CHD predicted risk among extremely obese adults prior to bariatric surgery. In this large multi-center cohort study, more than 1/3 of bariatric surgery candidates without prevalent CVD had high 10-year CHD predicted risk, but most bariatric surgery candidates with low 10-year CHD predicted risk had high lifetime CVD predicted risk. Low 10-year/high lifetime CVD risk was more common among women and younger men, but was not associated with BMI, waist circumference, HDL-C or hsCRP, suggesting that these factors may not adequately identify high lifetime CVD predicted risk among bariatric surgery candidates with low 10-year risk.

The prevalence of high 10-year risk in our study was 2-fold higher compared with the US population (36.5 vs. 18%),² primarily due to the higher prevalence of diabetes in our cohort. Diabetes predicts excess CVD risk in extreme obesity, even after adjusting for other CVD risk factors⁹ and bariatric surgery.¹⁰ Therefore, since our objective was to evaluate lifetime risk among bariatric surgery candidates with low 10-year CHD predicted risk, we followed the established ATP-III 10-year risk algorithm by considering bariatric surgery candidates with diabetes to not have low short-term CHD risk. Future studies should evaluate additional risk stratification and potential effects of bariatric surgery specifically among diabetic bariatric surgery patients, using outcome data and diabetes-specific risk scores.

Most LABS-2 participants without diabetes or prevalent CVD had low short-term, or 10-year CHD predicted risk, because most are non-smoking middle-aged women, with only moderately elevated total and LDL-C levels. In fact, our cohort had slightly lower LDL-C and TC levels than US population estimates,^{2,11} or previously reported bariatric surgery studies,¹² possibly reflecting secular risk factor improvements among bariatric surgery candidates or the broader US population,^{11,13} or a weaker association between lipid levels and BMI at high levels of BMI.^{14,15} Our results suggest that long follow-up will be needed to show a reduction in CVD events for bariatric surgery cohorts with a high prevalence of low 10-year CHD risk. Indeed, in the Swedish Obese Subjects (SOS) study of bariatric surgery patients and matched controls, CVD event curves did not diverge until 6 years follow-up, and a statistically significant reduction in total CVD was detected at a median follow-up of 14.7 years.¹⁰

However, as noted, most bariatric surgery candidates with low 10-year risk had high lifetime CVD predicted risk which was not associated with BMI, waist circumference, hsCRP, or HDL-C. Outcome studies have shown that BMI and waist circumference are not associated with CVD events independently of CVD risk factors among the general population,¹⁵ or among obese and extremely obese adults, with or without bariatric surgery.¹⁰ Typical of bariatric surgery patients,¹⁶ hsCRP levels were high, and hsCRP predicts CVD even at very high hsCRP levels (>10 mg/L), in the general population.¹⁷ Bariatric surgery decreases hsCRP along with weight loss,^{16,18} but associations between hsCRP and CVD events among bariatric surgery patients are not yet known. Finally, low HDL-C was only associated with high lifetime CVD predicted risk if added as a major risk factor, but doing so reclassified 15% of LABS-2 participants as high lifetime risk, compared with only 6.5% reclassified in US population estimates.² However, in SOS, higher baseline HDL-C was independently associated with lower risk for total MI, but not fatal MI or total CVD, and was positively associated with fatal stroke.¹⁰ Outcome data are needed to clarify the role of HDL-C in CVD risk stratification among extremely obese adults, with or without bariatric surgery.

Potential limitations of our study should be considered in interpreting our results. First, the use of a single measurement of SBP and DBP is not the gold-standard for diagnosing hypertension. However, the majority of hypertension in this study was defined by anti-hypertensive medication use, which should reduce misclassification. Diabetes was defined by self-report, but participants completed forms after complete medical workup for surgery. Misclassification of CVD risk factors would likely underestimate the prevalence of high 10 year or high lifetime predicted risk, which are already quite high in this sample, further emphasizing the need for long-term monitoring and appropriate treatment of CVD risk factors in this population. Sleep apnea status was not determined by routine diagnostic sleep studies on all participants, but was determined by clinical researchers using a combination of medical records (i.e., sleep study results) and participant report of prior sleep studies and CPAP use. While 81% of participants classified as having sleep apnea had either a positive sleep study or reported CPAP use, some misclassification is possible, which would likely have weakened the association between sleep apnea and risk strata. This study also had limited ability to evaluate differences by race-ethnicity given that only 14.2% of participants were non-white. Finally, the lifetime CVD risk prediction algorithm¹ focuses on atherosclerotic CVD and does not include lifetime risk of congestive heart failure, for which obesity and hypertension are major determinants. Indeed, a reduction in left ventricular mass with bariatric surgery has been reported with follow-up of up to 3 years.¹⁹

Bariatric surgery is highly effective for weight loss and for reducing diabetes,^{20,21} possibly even without weight loss depending on the type of surgery.²² Short-term bariatric surgery studies as well as the long-term follow-up of SOS have documented a reduction in CVD events,¹⁰ and reduced mortality, particularly from cancer.²³ Substantial reduction in triglycerides and low HDL-C have also been demonstrated over short and longer-term follow-up.^{12,18,24–26} However, there was no difference in the incidence of hypertension or the recovery from or incidence of hypercholesterolemia for bariatric surgery patients vs. matched controls in 10-year follow-up of SOS,²⁵ similar to long-term results from non-surgical weight loss trials.^{27–29} Associations between long-term changes in CV risk factors and CVD events should be evaluated among bariatric surgery patients, and the adequacy of existing risk stratification tools for bariatric surgery patients, especially post-surgery, should be tested using outcome data. However, the utility of pre-surgery risk factors and existing risk scores such as lifetime CVD predicted risk among adults with extreme obesity is supported by long-term outcome studies of obese adults showing that traditional CVD risk factors, not BMI, predict CHD and CVD, with¹⁰ or without^{9,10} bariatric surgery intervention. Our results highlight the opportunity to advise bariatric surgery candidates of their lifetime CVD predicted risk and the importance of long-term monitoring of cardiovascular risk factors, i.e., smoking, hypertension and lipids. Appropriate pharmacological or non-pharmacological treatment may be important even post-surgery to maximize reductions in cardiovascular disease.

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Figure.
Distribution of 10-Year and Lifetime CVD Predicted Risk by Age-Group and Sex among 2070 CVD-free LABS-2 Participants

Characteristics of Study Sample, Longitudinal Assessment of Bariatric Surgery-2 Participants without Prevalent cardiovascular Disease vs. Excluded Participants with Prevalent Cardiovascular Disease

Table 1

Variable	Study sample (No prevalent cardiovascular disease)			Excluded participants (with prevalent cardiovascular disease)	
	Total (n=2070)	Women (n=1665)	Men (n=405)	<i>P^a</i>	<i>P^b</i>
White	85.8 (0.8%)	84.3 (0.9%)	92.0 (1.4%)	<.001	0.65
Women	80.4 (0.9%)	-	-		<.001
Age (years)	45 (36.53)	44 (36.53)	46 (38.55)	<.01	<.001
Body mass index (kg/m ²)	45.8 (41.7,51.3)	45.6 (41.6,50.8)	47.2 (42.6,53.1)	<.001	0.16
Waist circumference (cm)	130.5 (120.8,142.3)	127.5 (118.5,137.5)	146.9 (136.0,158.6)	<.001	<.01
Diabetes mellitus	32.7 (1.0%)	30.5 (1.1%)	41.5 (2.5%)	<.001	<.001
Smoker	13.0 (0.7%)	13.6 (0.8%)	10.4 (1.5%)	0.08	0.65
Hypertension	57.5 (1.1%)	54.9 (1.2%)	68.4 (2.3%)	<.001	<.001
Systolic blood pressure (mmHg)	129 (120,139)	128 (120,138)	132 (122,143)	<.001	0.78
Diastolic blood pressure (mmHg)	80 (73,86)	80 (73,85)	80 (73,87)	0.10	<.001
Sleep Apnea	50.8 (1.1%)	45.5 (1.2%)	72.4 (2.2%)	<.001	<.001
High-sensitivity C-reactive protein (mg/L)	7.2 (4.1,13.5)	7.7 (4.5,14.4)	5.8 (2.9,9.1)	<.001	0.02
Anti-hypertensive medications	50.6 (1.1%)	48.5 (1.2%)	59.5 (2.4%)	<.001	<.001
Lipid-lowering medications	25.4 (1.0%)	23.1 (1.0%)	34.8 (2.4%)	<.001	<.001
Total cholesterol (mg/dL)	185 (161,211)	188 (163,214)	173 (151,199)	<.001	<.001
Total cholesterol 200 mg/dL	34.7 (1.1%)	37.1 (1.2%)	24.9 (2.2%)	<.001	0.02
Low density lipoprotein cholesterol (mg/dL)	109 (87,132)	111 (89,133)	101 (79,124)	<.001	<.001
Low density lipoprotein cholesterol 100 mg/dL	61.3 (1.1%)	63.7 (1.2%)	51.6 (2.5%)	<.001	<.001
High density lipoprotein cholesterol (mg/dL)	43 (37,51)	45 (38,53)	37 (32,42)	<.001	<.001
Low high density lipoprotein cholesterol ^c	66.1 (1.0%)	66.7 (1.2%)	63.7 (2.4%)	0.26	0.29
Non-high density lipoprotein cholesterol (mg/dL)	140 (116,165)	141 (117,166)	134 (111,161)	0.01	<.001
Non-high density lipoprotein cholesterol 130 mg/dL	60.6 (1.1%)	62.2 (1.2%)	54.1 (2.5%)	<.01	<.001
Triglycerides (mg/dL)	138 (100,192)	136 (98,190)	146 (109,200)	<.001	<.001
Triglycerides 150 mg/dL	42.8 (1.1%)	41.4 (1.2%)	48.4 (2.5%)	0.01	<.01

Values are median (interquartile range) or % (Standard Error).

^a *p* for women vs. men

p for study sample vs. excluded participants,

c Low high density lipoprotein cholesterol defined as <40 mg/dL men, <50 mg/dL women

Table 2

Distribution of Combined 10-Year Coronary Heart Disease and Lifetime Cardiovascular Disease Predicted Risk Strata among 2070 Cardiovascular Disease-Free Longitudinal Assessment of Bariatric Surgery-2 Participants, with High Density Lipoprotein Cholesterol Included as an Additional Major Risk Factor for Lifetime Cardiovascular Disease Predicted Risk

	Low 10-year coronary heart disease risk/ low lifetime cardiovascular disease risk	Low 10-year coronary heart disease risk/ high lifetime cardiovascular disease risk	High 10-year coronary heart disease risk/ high lifetime cardiovascular disease risk
Lifetime predicted cardiovascular disease risk- standard algorithm (high density lipoprotein cholesterol not included)	321, 15.5%	993, 48.0%	756, 36.5%
Lifetime predicted cardiovascular disease risk- with low high density lipoprotein cholesterol ^a as major risk factor	114, 5.5%	1200, 58.0%	756, 36.5%

Results are all N, %. 10-year hard coronary heart disease risk calculated based on Framingham Risk Score, with “low” defined as <10% 10-year predicted coronary heart disease risk and absence of diabetes mellitus.

^aLow high density lipoprotein cholesterol defined as <40 mg/dl for men and <50 mg/dl for women

Table 3

Characteristics^a of 2070 Cardiovascular Disease-Free Longitudinal Assessment of Bariatric Surgery-2 Participants According to 10-Year Coronary Heart Disease and Lifetime Cardiovascular Disease Predicted Risk Strata

	Low 10-year coronary heart disease predicted risk (total) (n=1314)	Low 10-year coronary heart disease/low lifetime cardiovascular disease predicted risk (n= 321)	Low 10-year coronary heart disease/high lifetime cardiovascular disease predicted risk (n=993)	High 10-year coronary heart disease predicted risk (n=756)	<i>p^b</i>	<i>p^c</i>	<i>p^d</i>
White	86.2 (1.0%)	88.4 (1.8%)	85.4 (1.1%)	85.1 (1.3%)	0.80	0.98	0.40
Women	86.3 (1.0%)	87.2 (1.9%)	86.0 (1.1%)	70.2 (1.7%)	<.001	<.001	0.58
Age, years	41 (34.50)	37 (31.44)	43 (35.52)	50 (42.57)	<.001	<.001	<.001
Body mass index, kg/m ²	45.6 (42.0,50.7)	45.4 (42.0,50.6)	45.6 (42.0,50.8)	46.4 (41.5,52.4)	0.18	0.22	0.93
Waist circumference, cm ^e	127.9 (119.0,138.1)	127.4 (118.8,138.1)	128.0 (119.0,138.1)	136.1 (125.0,147.0)	<.001	<.001	0.55
Diabetes mellitus	-	-	-	89.4 (1.1%)	-	-	-
Smoker	13.2 (0.9%)	-	17.4 (1.2%)	12.7 (1.2%)	0.76	<.01	<.001
Hypertension	45.8 (1.4%)	11.8 (1.8%)	56.8 (1.6%)	77.9 (1.5%)	<.001	<.001	<.001
Systolic blood pressure, mm/Hg	128 (120,138)	123 (116,129)	130 (121,141)	131 (122,142)	<.001	0.24	<.001
Diastolic blood pressure, mm/Hg	80 (74,86)	78 (73,83)	81 (75,88)	78 (71,85)	<.001	<.001	<.001
Sleep apnea	44.3 (1.4%)	39.9 (2.7%)	45.7 (1.6%)	62.0 (1.8%)	<.001	<.001	0.07
High-sensitivity C-reactive protein, mg/L ^f	7.5 (4.2,13.7)	8.0 (4.3,14.1)	7.4 (4.2,13.6)	7.0 (3.7,13.1)	<.01	0.02	0.50
Anti-hypertensive medications	37.4 (1.3%)	-	49.5 (1.6%)	73.7 (1.6%)	<.001	<.001	<.001
Lipid-lowering medications	12.7 (0.9%)	-	16.8 (1.2%)	47.4 (1.8%)	<.001	<.001	<.001
Total cholesterol, mg/dL	188 (164,212)	170 (153,185)	198 (170,220)	181 (153,210)	<.001	<.001	<.001
Total cholesterol 200 mg/dL	36.5 (1.3%)	0.0 (0.0)	48.3 (1.6%)	31.5 (1.7%)	0.02	<.001	<.001
Low density lipoprotein cholesterol, mg/dL	113.5 (93,134)	99 (84,114)	120 (97,141)	102 (78,127)	<.001	<.001	<.001
Low density lipoprotein cholesterol 100 mg/dL	66.2 (1.3%)	49.5 (2.8%)	71.6 (1.4%)	52.8 (1.8%)	<.001	<.001	<.001
High density lipoprotein cholesterol, mg/dL	44 (38,53)	43 (38,51)	45 (38,53)	41 (35,48)	<.001	<.001	0.40
Low high density lipoprotein cholesterol, mg/dL ^g	62.3 (1.3%)	64.5 (2.7%)	61.6 (1.5%)	72.6 (1.6%)	<.001	<.001	0.36
Non-high density lipoprotein cholesterol, mg/dL	141 (119,164)	124 (106,139)	150 (124,172)	137.5 (110,166)	0.03	<.001	<.001
Non-high density lipoprotein cholesterol 130 mg/dL	62.6 (1.3%)	40.8 (2.7%)	69.6 (1.5%)	57.1 (1.8%)	0.02	<.001	<.001

		Low 10-year coronary heart disease predicted risk (total) (n=1314)	Low 10-year coronary heart disease/low lifetime cardiovascular disease predicted risk (n= 321)	Low 10-year coronary heart disease/high lifetime cardiovascular disease predicted risk (n=993)	High 10-year Coronary heart disease predicted risk (n=756)	<i>p^b</i>	<i>p^c</i>	<i>p^d</i>
Triglycerides, mg/dL		129 (94,174)	102 (80,142)	135 (100,182)	162 (116,227)	<.001	<.001	<.001
Triglycerides 150 mg/dL		35.2 (1.3%)	21.2 (2.3%)	39.8 (1.6%)	56.0 (1.8%)	<.001	<.001	<.001

10-year Adult Treatment Panel-III hard coronary heart disease risk, with “low” defined as <10% and absence of diabetes mellitus.

^a Values are median (interquartile range) or percentage (standard error),

^b low 10-year vs. high 10-year,

^c low 10-year/high lifetime vs. high 10-year,

^d low 10-year/low lifetime vs. low 10-year/high lifetime,

^e waist circumference missing=95,

^f high-sensitivity C-reactive protein missing=3,

^g Low high density lipoprotein cholesterol <40 mg/dl in men and <50 mg/dl in women