Apolipoprotein B and non-high density lipoprotein cholesterol and the risk of coronary heart disease in Chinese

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Abstract The aim of our study was to compare apolipoprotein B (apoB), non-high density lipoprotein cholesterol (nonHDL-C), low density lipoprotein cholesterol (LDL-C), and other lipid markers as predictors of coronary heart disease (CHD) in Chinese. Overall, 122 individuals developed CHD during a median 13.6 years of follow-up in 3,568 adult participants from a community-based cohort. The multivariate relative risk of CHD in the highest quintile compared with the lowest quintile was 2.74 [95% confidence interval (CI), 1.45–5.19] for apoB, 1.98 (95% CI, 1.00–3.92) for nonHDL-C, and 1.86 (95% CI, 1.00–3.49) for LDL-C (all tests for trend, $P < 0.05$). ApoB also had the highest receiver operator characteristic curve area (0.63; 95% CI, 0.58–0.68) in predicting CHD. When apoB and nonHDL-C were mutually adjusted, only apoB was predictive; the relative risk was 2.80 (95% CI, 1.31–5.96; $P = 0.001$) compared with 1.09 (95% CI, 0.49–2.40; $P = 0.75$) for nonHDL-C. Compared with the lowest risk, participants with the highest apoB and total cholesterol/HDL-C had a 3-fold increased risk of developing CHD (relative risk = 3.21; 95% CI, 1.45–7.14). These data provide strong evidence that apoB concentration was a better predictor of CHD than other lipid markers in Chinese.—Chien, K-L., H-C. Hsu, T-C. Su, M-F. Chen, Y-T. Lee, and F. B. Hu. **Apolipoprotein B and non-high density lipoprotein cholesterol and the risk of coronary heart disease in Chinese. *J. Lipid Res.* 2007.** 48: **2499–2505.**

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Increased low density lipoprotein cholesterol (LDL-C) concentrations are a well-established risk factor for coronary heart disease (CHD) and are currently recommended as the primary target for lipid-lowering therapy for the prevention and treatment of cardiovascular disease) (1). However, recent evidence suggests that apolipoproteins, especially apolipoprotein B (apoB), may be more strongly associated with CHD incidence than LDL (2, 3). Apolipoprotein plays a role in transporting lipid particles and is considered a direct measurement of proatherogenic particles (3, 4). In addition, non-high density lipoprotein cholesterol (nonHDL-C; calculated as the difference between total cholesterol and HDL cholesterol), reflecting the cholesterol concentration of all atherogenic lipoproteins, has also been demonstrated to predict CHD risk (5, 6). NonHDL-C has been recommended as a target for primary prevention among patients with diabetes or high triglyceride (TG) levels (1, 7). However, the superiority of LDL-C, apoB, and nonHDL-C in predicting CHD remains unsettled (8, 9). Furthermore, to our knowledge, no previous study has directly compared the predictive capacity of these biomarkers in Asian populations. Therefore, we conducted a prospective study to examine the role of apoB, nonHDL-C, and LDL-C in predicting CHD incidence among ethnic Chinese in Taiwan.

METHODS

Study design and study population

Details of this cohort study have been published previously (10–12). Briefly, the Chin-Shan Community Cardiovascular Cohort Study began in 1990 by recruiting 1,703 men and 1,899 women ≥35 years old, homogeneous in Chinese ethnicity, and living in the Chin-Shan township 30 km north of metropolitan

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Abbreviations: apoB, apolipoprotein B; CHD, coronary heart disease; LDL-C, low density lipoprotein cholesterol; nonHDL-C, non-high density lipoprotein cholesterol; ROC, receiver operator characteristic; TC, total cholesterol; TG, triglyceride.

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Taipei, Taiwan. Information about anthropometry, lifestyle, and medical conditions was assessed by interview questionnaires in 2 year cycles, and the validity and reproducibility of the collected data and measurements have been reported in detail elsewhere (12). In follow-up of the cohort through 2005 (median 13.6 years), we identified 122 incident cases of CHD (79 men, 43 women), defined as nonfatal myocardial infarction, fatal CHD, or hospitalization for percutaneous coronary intervention and coronary bypass surgery. Deaths were identified from official death certificates and further verified by house-to-house visits. Fatal CHD was considered to have occurred if there was fatal myocardial infarction confirmed by hospital records, or if CHD listed as the cause of death on the death certificate was the underlying and most plausible cause of death, or if evidence of previous CHD was available. The National Taiwan University Hospital Committee Review Board approved the study protocol. All participants provided oral informed consent when they were recruited into the study in 1990.

All venous blood samples drawn after a 12 h overnight fast were immediately refrigerated and transported within 6 h to National Taiwan University Hospital. Serum samples were then stored at −70°C before batch assay for levels of total cholesterol (TC), TG, HDL-C, apoA-I, and apoB. Standard enzymatic tests for serum cholesterol and TG were used (Merck 14354 and 14366, respectively). HDL-C levels were measured in supernatants after the precipitation of specimens with magnesium chloride phosphotungstate reagents (Merck 14993). LDL-C concentrations were calculated as TC minus cholesterol in the supernatant by the precipitation method (Merck 14992). ApoA-I and apoB concentrations were measured by turbidimetric immunoassay with commercial kits (Sigma). NonHDL-C was calculated by subtracting HDL-C from TC. A total of 3,568 participants with blood

TABLE 1. Distribution of various baseline demographic, lifestyle, and socioeconomic factors in the study population in the CCCC (1990–1991), specified by apoB quintiles

	Quintiles					
Variable	1 (n = 721)	2 (n = 682)	3 (n = 700)	4 (n = 680)	5 (n = 685)	*P*
			%			
Women	51.0	55.9	48.7	55.7	55.9	0.013
Age (years)						<0.0001
35–44	30.6	28.7	24.0	23.1	19.4	
45–54	25.7	23.7	25.0	25.6	25.7	
55–64	22.6	24.0	29.0	27.4	27.2	
65–74	13.6	14.3	17.3	19.0	19.7	
≥75	7.5	9.4	4.7	5.0	8.0	
Body mass index (kg/m^2)						<0.0001
<18	6.5	3.8	3.7	2.4	1.8	
18–20.9	29.5	23.3	18.5	16.0	10.7	
21–22.9	28.8	25.9	24.1	23.2	20.4	
23–24.9	19.1	20.9	21.7	23.8	23.3	
≥25	16.2	26.1	32.0	34.7	43.8	
Current smoker (yes)	36.8	33.3	38.3	36.0	35.0	0.378
Alcohol drinking (yes)	29.4	25.8	31.6	30.6	30.5	0.157
Marital status						0.003
Single	4.2	2.5	3.0	1.8	2.5	
Living with spouse	86.4	86.0	88.6	84.2	83.9	
Divorced or separated	9.5	11.5	8.4	14.0	13.6	
Education level						0.938
<9 years	94.7	94.6	94.1	94.3	93.7	
≥9 years	5.3	5.4	5.9	5.7	6.3	
Job status						0.000
No job	46.5	50.9	48.0	52.2	54.7	
Blue collar	39.9	34.6	36.0	31.3	27.0	
White collar	13.6	14.5	16.0	16.5	18.3	
Regular exercise (yes)	12.6	14.8	15.4	15.4	16.4	0.354
Family history of CHD	9.0	8.1	10.0	9.6	11.7	0.228
Hypertension	21.5	27.3	28.2	32.3	43.0	<0.0001
Diabetes mellitus	8.8	9.1	12.0	17.0	19.9	<0.0001

Variable	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	*P*
Age	53.6	12.6	54.6	13.2	54.8	11.7	55.1	11.7	56.6	12.1	0.0002
Body mass index	22.2	3.1	23.1	3.3	23.6	3.4	24.0	3.5	24.6	3.4	<0.0001
Lipid profiles											
TC	163.3	31.9	185.3	32.8	197.3	37.4	210.6	40.1	234.1	48.3	<0.0001
TG	93.4	81.1	103.6	78.4	118.8	84.2	138.3	92.3	178.7	113	<0.0001
HDL-C	51.4	13.1	49.6	13.5	47.6	13.6	45.1	10.8	43.4	10.4	<0.0001
LDL-C	100.4	29.1	124.0	29.6	137.8	34.2	152.5	37.0	176.5	46.6	<0.0001
NonHDL-C	111.7	30.1	135.7	30.7	149.4	35.4	165.4	38.8	190.5	47.5	<0.0001
TC/HDL-C	3.34	1.01	3.96	1.10	4.41	1.34	4.89	1.36	5.64	1.58	<0.0001
ApoA-I	129.3	29.4	128.8	26.2	131.4	26.7	136.8	58.0	141.8	27.2	<0.0001
ApoB	56.5	9.1	75.2	4.3	90.6	4.6	108.6	6.3	144.0	21.1	<0.0001
ApoB/apoA-I	0.46	0.12	0.61	0.13	0.72	0.15	0.83	0.16	1.05	0.22	<0.0001

ApoB apolipoprotein B; CCCC, Chin-Shan Community Cardiovascular Cohort; CHD, coronary heart disease; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; nonHDL-C, non-high density lipoprotein cholesterol; TC, total cholesterol; TG, triglyceride.

TABLE 2. Age- and gender-adjusted Spearman partial correlation coefficients between various lipid profiles among the study subjects in the CCCC

Lipid	TG	HDL-C	LDL-C	NonHDL-C	TC/HDL-C	ApoA-I	ApoB	ApoB/ApoA-I
TC	0.27[a]	0.09[a]	0.94[a]	0.95[a]	0.57[a]	0.12[a]	0.55[a]	0.45[a]
TG		−0.48[a]	0.39[a]	0.41[a]	0.58[a]	−0.08[a]	0.44[a]	0.48[a]
HDL-C			−0.17[a]	−0.19[a]	−0.73[a]	0.62[a]	−0.24[a]	−0.58[a]
LDL-C				0.98[a]	0.76[a]	−0.05[b]	0.62[a]	0.61[a]
NonHDL-C					0.78[a]	−0.06[a]	0.62[a]	0.62[a]
TC/HDL-C						−0.41[a]	0.57[a]	0.79[a]
ApoA1							0.20[a]	−0.34[a]
ApoB								0.83[a]

[a] $P < 0.001$.
[b] $P < 0.01$.

lipid data and free from cardiovascular disease at baseline were included in the study.

Statistical analysis

Participants were categorized on the basis of quintile of apoB levels, and continuous variables are presented by mean, standard deviation, or median levels; categorical data are presented in contingency tables, with ANOVA to test for differences among quintiles. Relationships between lipid marker levels were examined by the age- and gender-adjusted Spearman's partial correlation coefficients.

CHD incidence rates were calculated by person-year methods and stratified by various lipid marker quintiles. We analyzed the association between lipid levels and risk of CHD using the Cox regression model, adjusting for potential confounding factors. The proportionality assumption and the fit of the proportional hazards model were verified by the Grambsch and Therneau sta-

TABLE 3. Relative risks (and 95% CI values) of CHD during a median 13.6 years of follow-up according to quintiles of baseline lipid profiles in 1990–1991 in the CCCC study

	1	2	3	4	5	Trend Test
TC	145	172	193	217	258	
Incidence rate	2	1.8	3.3	2.4	4	
Model 1	1	0.91(0.46—1.78)	1.65(0.91—2.98)	1.15(0.61—2.15)	1.93(1.08—3.44)	0.014
Model 2	1	0.91(0.46—1.80)	1.54(0.84—2.82)	1.02(0.54—1.94)	1.64(0.90—2.97)	0.08
TG	54	76	99	133	231	
Incidence rate	1.4	2.8	2.1	2.7	4.5	
Model 1	1	1.88(0.96—3.66)	1.43(0.71—2.90)	1.80(0.91—3.57)	3.13(1.66—5.87)	0.000
Model 2	1	1.74(0.89—3.39)	1.15(0.56—2.35)	1.19(0.59—2.41)	2.05(1.06—3.97)	0.07
HDL-C	64	53	46	41	33	
Incidence rate	1.6	1.4	2.2	3.2	4.9	
Model 1	1	0.73(0.46—1.17)	0.51(0.30—0.89)	0.33(0.17—0.63)	0.39(0.21—0.71)	<.0001
Model 2	1	0.85(0.53—1.38)	0.63(0.36—1.11)	0.45(0.23—0.86)	0.55(0.29—1.04)	0.013
LDL-C	87	112	134	158	197	
Incidence rate	1.8	1.6	2.7	2.8	4.7	
Model 1	1	0.88(0.43—1.80)	1.48(0.78—2.79)	1.57(0.83—2.97)	2.50(1.38—4.51)	0.000
Model 2	1	0.80(0.38—1.67)	1.31(0.68—2.52)	1.27(0.65—2.47)	1.86(1.00—3.46)	0.008
NonHDL-C	97	124	145	170	211	
Incidence rate	1.5	2.1	2.4	3	4.5	
Model 1	1	1.26(0.62—2.56)	1.51(0.75—3.05)	1.87(0.96—3.65)	2.71(1.43—5.15)	0.000
Model 2	1	1.16(0.56—2.41)	1.29(0.62—2.67)	1.51(0.75—3.05)	1.98(1.00—3.92)	0.016
TC/HDL-C	2.8	3.5	4.2	5	6.4	
Incidence rate	1	1.7	2	3.3	5.5	
Model 1	1	1.60(0.70—3.67)	1.89(0.84—4.21)	3.05(1.44—6.48)	4.38(2.14—8.98)	<.0001
Model 2	1	1.58(0.69—3.65)	1.59(0.70—3.61)	2.38(1.09—5.19)	3.04(1.42—6.50)	0.001
ApoA-I	169	146	131	117	101	
Incidence rate	1.4	2.4	3.1	3.1	3.4	
Model 1	1	1.02(0.61—1.72)	1.09(0.64—1.86)	0.91(0.51—1.62)	0.54(0.27—1.06)	0.08
Model 2	1	1.17(0.69—2.00)	1.30(0.75—2.25)	1.08(0.60—1.94)	0.68(0.34—1.36)	0.32
ApoB	58	75	91	108	139	
Incidence rate	1.6	1.9	1.8	3	5.3	
Model 1	1	1.22(0.60—2.47)	1.13(0.55—2.31)	1.92(1.00—3.68)	3.38(1.85—6.20)	<.0001
Model 2	1	1.18(0.57—2.44)	1.03(0.49—2.16)	1.67(0.85—3.30)	2.74(1.45—5.19)	<.0001
ApoB/apoA-I	0.43	0.57	0.69	0.84	1.07	
Incidence rate	1.5	1.6	2	2.1	6.4	
Model 1	1	1.02(0.48—2.16)	1.29(0.63—2.63)	1.27(0.62—2.60)	3.57(1.95—6.57)	<.0001
Model 2	1	0.91(0.43—1.95)	1.10(0.53—2.28)	0.89(0.42—1.88)	2.61(1.38—4.95)	<.0001

CI, confidence interval. Incidence rates are presented per 1,000 person-years. Model 1: adjusted for age groups (35–44, 45–54, 55–64, 65–74, or ≥75 years old) and gender. Model 2: as for model 1 plus body mass index (<18, 18–20.9, 21–22.9, 23–24.9, or ≥25 kg/m^2), smoking (yes/no or abstinence), current alcohol drinking (regular/no), marital status (single, married and living with spouse, or divorced and living separately), education level (<9 years, at least 9 years), occupation (no work, labor, official, or business), regular exercise habit (yes/no), family history of CHD (yes/no), baseline hypertension (yes/no), and diabetes mellitus (yes/no).

tistics (13). We specified two Cox models to evaluate the adjusted relative risks of quintile values. Model 1 was adjusted for age groups (35–44, 45–54, 55–64, 65–74, and ≥75 years old) and gender only. Model 2 included additional confounding factors: body mass index (<18, 18–20.9, 21–22.9, 23–24.9, or ≥25 kg/m^2), smoking (yes/no or abstinence), current alcohol drinking (regular/no), marital status (single, married and living with spouse, or divorced and living separately), education level (<9 years, at least 9 years), occupation (no work, labor, office, or business), regular exercise habit (yes/no), family history of CHD (yes/no), baseline hypertension (yes/no, defined by blood pressure of at least 140/90 mm Hg or on medication), and diabetes mellitus (yes/no, defined by fasting plasma glucose of at least 126 mg/dl or on medication). To test for linear trends across lipid marker categories, we used the median lipid profile levels within quintiles as a continuous variable. We also tested the goodness of fit of the model using the Hosmer and Lemeshow test (14).

We used the area under the curve of the receiver operator characteristic (ROC curve) to compare the discriminative ability of various risk factors (15). The area under the ROC curve was considered a global performance indicator for a prognostic factor (16). In addition, likelihood ratio test statistics were used to compare model fitting. We compared models with and without the four dummy lipid profiles and conducted likelihood ratio tests between nested models.

All statistical tests were two-tailed, and $P < 0.05$ was considered statistically significant. Analyses were performed with SAS version 9.1 (SAS Institute, Cary, NC) and Stata version 9.1 (Stata Corp., College Station, TX).

RESULTS

Participants with higher apoB levels were more likely to be female and older. They were more likely to have higher body mass index, hypertension, diabetes mellitus, higher levels of TC, TG, LDL-C, nonHDL-C, TC/HDL-C, apoA-I, and apoB/apoA-I, and significantly lower levels of HDL-C. There were no statistical differences in lifestyle factors such as smoking, alcohol consumption, and exercise habits across various apoB quintiles (**Table 1**).

We found strong correlations among TC, LDL-C, nonHDL-C, and TC/HDL-C, ranging from 0.76 to 0.98 (**Table 2**). HDL-C was inversely associated with other lipid markers, except with apoA-I ($r = 0.62$). The correlations of apoB with other lipid markers were moderate, ranging from 0.20 to 0.62.

Table 3 shows the relative risks of CHD during a median 13.6 years of follow-up across quintiles of lipid levels at baseline. After multivariate adjustment, the lipid ratios, such as TC/HDL-C and apoB/apoA-I, had the strongest associations with CHD (relative risks in the highest quintile = 3.04 and 2.61). Among single lipid markers, apoB showed the strongest association with CHD (relative risk = 2.74). NonHDL-C was also strongly predictive of CHD, with a multivariate risk similar to that of LDL (i.e., 1.98 vs. 1.86). The association of HDL-C with CHD was similar to that seen with LDL; participants in the lowest quintile had a 1.81-fold (1/0.55) higher risk of CHD than those in the highest quintile. **Figure 1** shows the cumulative CHD event-free rates according to quintiles of apoB and nonHDL-C. Compared with those in the lower quintiles, participants with the highest apoB or nonHDL-C quintile had significantly lower CHD event-free rates.

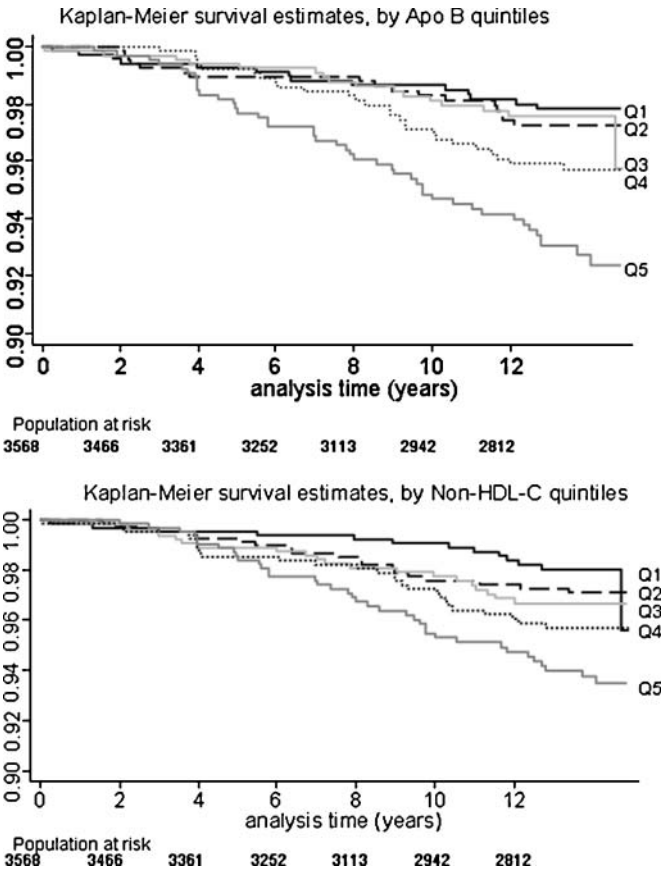

Fig. 1. Cumulative coronary heart disease (CHD) event-free rates according to quintiles of apolipoprotein B (apoB) (upper) and non-high density lipoprotein cholesterol (nonHDL-C) (lower).

To determine the predictive values of various lipid markers, we estimated the ROC curves and performed likelihood ratio tests. Except for lipid ratios (TC/HDL-C and apoB/apoA-I), both apoB and HDL-C showed greater ROC and likelihood ratio Chi-square values than TC, TG, LDL, or nonHDL-C (**Table 4**).

In mutually adjusted models, apoB and apoB/apoA-I remained significant and strong risk factors for CHD, whereas other lipid variables became nonsignificant (**Table 5**). In joint analyses, participants in the highest tertile of both apoB and TC/HDL ratio had >3-fold greater risk of CHD than those in the lowest tertiles of both variables (**Fig. 2**).

DISCUSSION

In this prospective cohort of middle-aged to older ethnic Chinese, higher levels of apoB were strongly and independently associated with increased future risk of CHD. ApoB appeared to be a stronger predictor of CHD risk than LDL or nonHDL-C. ApoB provided additional predictive power beyond the TC/HDL ratio.

TABLE 4. Area under the ROC curve and likelihood ratio test of various lipid profiles for CHD among the study subjects in the CCCC (1990–2005)

Lipid	Area under the ROC Curve	95% CI	Likelihood Ratio Test
TC	0.58	0.52–0.63	11.8
TG	0.59	0.54–0.64	17.0
HDL-C	0.62	0.57–0.68	26.7
LDL-C	0.60	0.55–0.65	17.9
NonHDL-C	0.60	0.55–0.65	16.3
TC/HDL-C	0.65	0.60–0.70	37.2
ApoA-I	0.57	0.52–0.62	9.0
ApoB	0.63	0.58–0.68	26.6
ApoB/apoA-I	0.66	0.60–0.71	44.1

ROC, receiver operator characteristic. Area under the ROC curve values are for a univariate model, with four dummy variables in the model. The likelihood ratio test compared the model with the corresponding marker and the model without the corresponding marker with 4 degrees of freedom.

Our results are consistent with previous studies conducted in primarily white populations (17). In the Health Professionals' Follow-Up Study conducted in the United States, apoB appeared to be the strongest predictor of CHD among individual lipid factors (17). After adjustment for matching factors, the relative risk of CHD in the highest quintile compared with the lowest quintile was 2.76 [95% confidence interval (CI), 1.66–4.58] for nonHDL-C, 3.01 (95% CI, 1.81–5.00) for apoB, and 1.81 (95% CI, 1.12–2.93) for LDL-C. As in our study, when apoB and nonHDL or LDL were mutually adjusted, only apoB remained statistically significant. Three other studies have also found strong and independent effects of apoB (18–20).

ApoB is synthesized by the liver, and because there is one apoB molecule in each lipoprotein particle, apoB reflects the total number of chylomicrons, VLDL, intermediate density lipoprotein, and LDL particles and can be viewed as total atherogenic burden (3). In our study, apoB was significantly related to CHD risk even after adjustment for other lipid markers, such as LDL-C and nonHDL-C values, despite its correlations with these markers.

Several studies have also suggested that nonHDL-C level is a better predictor of CHD than LDL-C level. In a sample of diabetic men, Jiang et al. (5) found that, after adjustment for age, body mass index, and other lifestyle risk factors, the multivariate relative risk of cardiovascular disease (the highest vs. the lowest quartile) was 2.34 (95% CI, 1.26–4.32) for nonHDL-C, 2.31 (95% CI, 1.23–4.35) for apoB, and 1.74 (95% CI, 0.99–3.06) for LDL cholesterol. The ROC areas were similar for apoB and nonHDL, and both were greater than for LDL-C. NonHDL-C has also been shown to be a strong predictor of cardiovascular disease risk in diabetic patients in two other studies. In the Strong Heart Study cohort, nonHDL-C was a stronger predictor of cardiovascular disease than LDL-C in 2,108 American Indian men and women aged 45–74 years with diabetes during an average of 9 years of follow-up (7). In a Finnish cohort study of 1,059 middle-aged men and women with type 2 diabetes, higher levels of nonHDL-C, as well as low HDL-C and TGs, were each independently associated with a 2-fold increased risk of CHD mortality during 7 years of follow-up (21). But these two studies did not compare the predictive values of apoB and nonHDL-C.

In our study, nonHDL-C was superior to LDL-C in predicting CHD risk, consistent with other studies (5, 22). Because nonHDL-C is easily calculated and highly correlated with apoB, it has been suggested that nonHDL-C can be substituted for apoB as a predictor of CHD risk (8, 23). However, our data showed that apoB was more strongly related to CHD risk than was nonHDL-C. Several subclinical disease studies provided evidence that apoB was superior to nonHDL-C in reflecting carotid and coronary artery atherosclerosis burden (24, 25). Our results support the hypothesis that direct measurement of the atherogenic particles (apoB concentration) is more biologically meaningful than the measurement of the cholesterol concentration in these particles (nonHDL-C concentration) (3, 17, 26). Neither nonHDL-C nor apoB measurements require fasting samples. In clinical practice, nonHDL-C is a simpler and more familiar approach to quantify all

TABLE 5. Combination of two lipid profiles adjusted for confounding factors in multivariable-adjusted models in the subjects

	Lipid 1				Lipid 2			
Model	Marker	Relative Risk	95% CI	*P* for Trend	Marker	Relative Risk	95% CI	*P* for Trend
1	ApoB	2.80	1.31–5.96	0.001	NonHDL-C	1.09	0.49–2.40	0.75
2	ApoB	2.21	1.07–4.56	0.003	TC/HDL-C	2.01	0.87–4.64	0.09
3	ApoB	2.68	1.38–5.21	0.000	HDL-C	1.57	0.83–2.98	0.06
4	ApoB	2.84	1.32–6.13	0.001	LDL-C	1.01	0.48–2.11	0.60
5	ApoB	2.86	1.46–5.62	0.000	TG	1.23	0.61–2.51	0.59
6	ApoB/apoA-I	2.67	1.23–5.77	0.000	NonHDL-C	1.12	0.50–2.50	0.91
7	ApoB/apoA-I	2.48	1.17–5.26	0.000	TC/HDL-C	1.12	0.54–2.35	0.69
8	ApoB/apoA-I	2.48	1.17–5.26	0.000	HDL-C	1.12	0.54–2.35	0.69
9	ApoB/apoA-I	2.65	1.22–5.73	0.001	LDL-C	1.08	0.51–2.25	0.69
10	ApoB/apoA-I	2.77	1.41–5.44	0.000	TG	1.32	0.65–2.67	0.51
11	ApoB/apoA-I	2.68	1.35–5.33	0.000	TC	1.08	0.55–2.12	0.88
12	NonHDL-C	1.77	0.89–3.53	0.035	HDL-C	1.71	0.9–3.24	0.02
13	NonHDL-C	0.87	0.35–2.19	0.91	TC/HDL-C	3.41	1.24–9.37	0.02

Results are from separate models of each combination of lipid profiles. Relative risk and 95% CI values are for the highest compared with the lowest quintile of each lipid profile. *P* for trend across quintiles of each profile was tested by replacing the median value as each quintile. Each lipid profile was added to the model in the quintile with four dummy variables. Adjustments were for age, gender, body mass index, family history of CHD, diabetes, hypertension, alcohol intake, smoking, exercise habit, marital status, education, and job status.

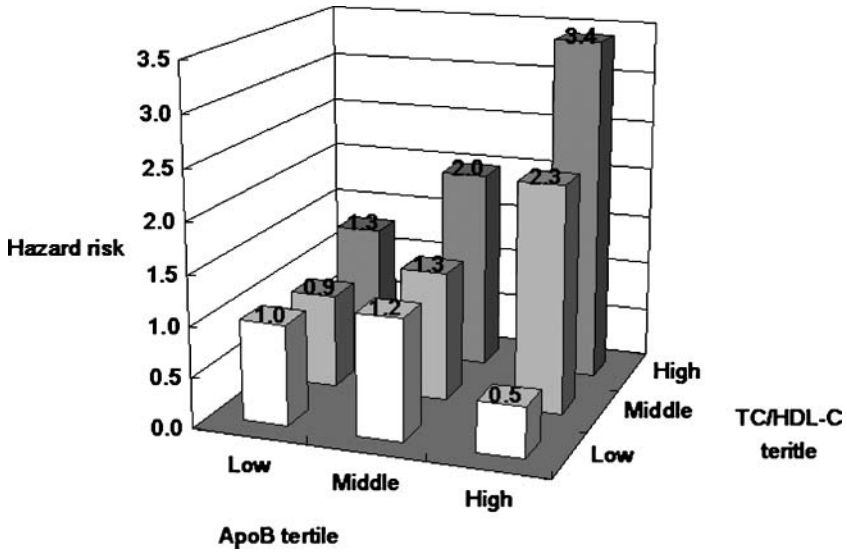

Fig. 2. Hazard risks of CHD during a median 13.6 years of follow-up according to tertiles of apoB and total cholesterol (TC)/HDL-C levels, adjusted for age, gender, body mass index, family history of CHD, diabetes, hypertension, alcohol intake, smoking, exercise habit, marital status, education, and job status. Cutoff points for tertiles of apoB were <77, 77–104, and ≥104 mg/dl. Cutoff points for tertiles of TC/HDL-C were <3.62, 3.62–4.80, and ≥4.80.

atherogenic lipoproteins. However, the methodology for measuring apoB has been standardized and is becoming more widely available (9).

To our knowledge, this is the first extensive investigation of various lipid markers and risk of CHD among ethnic Chinese. Evidence from other Asian populations also demonstrates that atherogenic particles play an important role in predicting CHD events, (27–31), but the head-to-head comparison of nonHDL-C and apoB has not been available. Because of the prospective cohort design, the baseline measurements of all cohort members were unlikely to be affected by storage and laboratory issues that might be raised in some nested case-control studies. The use of a community-based population could reduce the possibility of selection bias. We also included important socioeconomic status and lifestyle factors in the models to control for potential confounding factors. Finally, because few participants (<1%) reported taking cholesterol-lowering medications, our results were minimally affected by statins and other cholesterol-lowering drugs.

Our study had several potential limitations. First, the incident cases of CHD events were relatively few, even with a median 13.6 years of follow-up, which would reduce the power to detect subtle differences between various lipid markers and make the relative risk estimation unstable. However, the 95% CI values for the estimated relative risks were narrow and tests for linear trends were significant for most lipid variables. Second, because lipid levels were measured only once, our results might be attenuated by intraindividual variations.

In conclusion, we clearly demonstrate that apoB is more strongly associated than LDL-C with risk of CHD among ethnic Chinese. Our data indicate that apoB, a marker of LDL-carrying particles, should be taken into consideration in Asian populations, in addition to other lipid markers such as nonHDL-C. Because of only moderate correlation coefficients between apoB and other lipid markers (~0.2–0.6), we recommended that apoB be measured for comprehensive evaluation of CHD risk in Asian populations.

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