Blood Cholesterol Screening

Influence of Fasting State on Cholesterol Results and Management Decisions

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OBJECTIVE: **To compare fasting and nonfasting total and high-density lipoprotein (HDL) cholesterol values in adults and to determine how closely classification into risk groups for coronary heart disease based on nonfasting blood tests compares with classification based on fasting studies.**

DESIGN: **Cross-sectional study.**

SETTING: **A community hospital general internal medicine clinic.**

PATIENTS: **One hundred eighty-one patients at least 20 years of age receiving medical care at a community hospital general internal medicine clinic.**

INTERVENTIONS: **Total and HDL cholesterol levels were measured twice in each patient within 7 days, once while not fasting and once after a minimum 12-hour fast.**

MEASUREMENTS AND MAIN RESULTS: **Fasting and nonfasting total and HDL cholesterol values were compared, patients were classified into desirable, borderline-high, and high cholesterol groups on the basis of fasting and nonfasting blood studies. There were small, statistically significant but clinically insignificant differences in fasting and nonfasting results for total cholesterol. Nonfasting HDL cholesterol levels were similar to fasting HDL levels. The agreement in classification of patients into desirable and high-cholesterol groups between fasting and non-fasting blood testing was 86.7% and 89.5%, respectively. In the borderline-high group, for whom levels of HDL cholesterol are important in determining subsequent management, there was 95% agreement between fasting and nonfasting HDL cholesterol results. Only a small fraction of the patients were classified into lower-risk groups by the nonfasting assessment, creating the potential for less-rigorous monitoring and treatment of their cholesterol status than if fasting results were utilized. These findings were confirmed in this study also for the subgroups of men aged 35 years and older and women aged 45 years and older.**

CONCLUSIONS: **Screening nonfasting adults for total and HDL cholesterol is appropriate for making decisions about primary prevention of coronary heart disease.**

KEY WORDS: **cholesterol; screening; fasting; hypercholesterolemia.**
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The Second Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel II [ATP II]) confirmed that an elevated blood cholesterol level increases the risk of coronary heart disease and presented clinical guidelines on cholesterol management for health care professionals.[1,2] It also used total and high-density lipoprotein (HDL) cholesterol levels to define risk groups and made specific recommendations for primary prevention in adults without evidence of coronary heart disease and for secondary prevention in adults with evidence of coronary heart disease. The report specified that serum total and HDL cholesterol levels should be measured in all adults age 20 years and older at least every 5 years and advised that these measurements may be made in the nonfasting state. Other advisory groups like the United States Preventive Services Task Force (USPSTF)[3] and the American College of Physicians (ACP)[4] agree with these recommendations for periodic total and HDL cholesterol screening but advise that this testing not be initiated until age 35 in men and age 45 in women.

Adults without evidence of coronary heart disease and with total cholesterol level less than 200 mg/dL (5.18 mmol/L) are classified as having *desirable blood cholesterol*, and only further screening of total cholesterol and HDL cholesterol levels at least once every 5 years is recommended. Individuals free of coronary heart disease and with total cholesterol level equal to or greater than 240 mg/dL (6.22 mmol/L) are classified as having *high blood cholesterol.* Twenty percent of the U.S. adult population have high blood cholesterol according to the third National Health and Nutrition Examination Survey.[5] Fasting lipoprotein analysis with improved accuracy in the measurement of total cholesterol, HDL cholesterol, triglyceride, and calculated low-density lipoprotein (LDL) cholesterol levels is recommended to guide management decisions for these individuals. Individuals free of coronary heart disease with total cholesterol level from 200 to 239 mg/dL (5.18 to 6.22 mmol/L) are classified as having *borderline-high blood cholesterol*. For these individuals, the level of HDL cholesterol and the presence of other risk factors for heart disease determine the recommended follow-up. If HDL cholesterol is less than 35 mg/dL (0.91 mmol/L), or 2 or more additional risk factors for heart disease are present, a fasting lipoprotein analysis is recommended. If HDL cholesterol level equals or exceeds 35 mg/dL (0.91 mmol/L) and fewer than 2 other risk factors are present, patients are instructed to modify their diet, increase physical activity, and have total and HDL cholesterol analyses repeated in 1 to 2 years.

Since the release of the expert panel's report,[1,2] questions about the accuracy of total cholesterol and HDL cholesterol measurements in nonfasting subjects have been raised. Previous investigations focused on assessing differences in fasting and postprandial cholesterol values obtained in small numbers of normal healthy volunteers fed either very high-fat liquid formulas,[6–9] or highly standardized high-fat meals,[10,11] in controlled laboratory settings. Blood specimens were obtained at well-defined intervals after ingestion. These studies have shown small differences in total and HDL cholesterol values and confirmed that high-fat test meals and short blood draw intervals after meal consumption increase these differences.

The present study was designed to compare fasting and nonfasting total cholesterol and HDL cholesterol values in adult patients attending a primary care general internal medicine clinic. The effects of age, gender, smoking, alcohol use, medication use, and comorbid conditions on cholesterol levels were investigated. Finding that fasting and nonfasting cholesterol values do not differ would support the recommendation of the expert panel that screening nonfasting adults for total and HDL cholesterol levels provides accurate data to guide decisions about primary prevention of coronary heart disease.

METHODS

Study Design

The study site was a general internal medicine physician clinic affiliated with the University of Iowa–Des Moines Internal Medicine Residency Program. After Institutional Review Board approval was obtained, men and women, at least 20 years of age, who were cared for by 2 general internal medicine faculty at this community hospital clinic location, were asked to participate in this cross-sectional study. A convenience sample design was used for patient enrollment. Patients were intermittently enrolled in the study on days when a part-time research nurse coordinator was available to enroll patients. On these days all patients were invited to participate. No information was obtained on those patients who declined to participate in the study. Patients were excluded if they were less than 20 years of age, had inadequate vein access for drawing blood, had a bleeding disorder that complicated venipuncture, or were taking lipid-lowering medications. After signing the approved informed consent form, each patient had 10 mL of blood drawn from an antecubital vein twice within 7 days, once when not fasting and once after a minimum 12-hour fast. Each patient then completed a brief questionnaire indicating tobacco use, alcohol use, medication use, and prior history of myocardial infarction, stroke, transient ischemic attack, diabetes mellitus, obesity, or hyperlipidemia. Patients were also asked to document their food intake for the 12 hours prior to each blood draw to ensure that blood specimens were obtained under the appropriate fasting and nonfasting conditions.

Blood Sample Analysis

Blood samples were immediately processed and analyzed for total and HDL cholesterol at the certified laboratory on site at the clinic. Total and HDL cholesterol were measured enzymatically on a Dade Paramax 720 ZX analyzer (Dade International, Miami, Fla). Total cholesterol level was measured using reagents supplied by the manufacturer. High-density lipoprotein cholesterol level was measured using reagents supplied by Sigma Diagnostics (St. Louis, Mo). For this laboratory, the coefficients of variation for total cholesterol and HDL cholesterol measurements were 2.7% and 5.6%, respectively.

Statistics

Paired *t* tests were used to determine if differences in fasting and nonfasting measurements for total cholesterol and HDL cholesterol levels were statistically significant. For each parameter, an intraclass correlation was computed for the pair of fasting and nonfasting assessments. Fasting and nonfasting assessments were used to classify participants into 1 of 3 groups: desirable, borderline-high, or high blood cholesterol. The agreement between the fasting and nonfasting measurements for each group was assessed with the κ statistic. Following the procedure used by Wilder et al.,[12] analyses were also conducted of the sensitivity and specificity of the nonfasting assessment of each parameter relative to the fasting assessment. Ninety-five percent confidence intervals (95% CIs) were calculated for these sensitivity and specificity results.

Finally, multiple regression analyses were conducted to evaluate whether the relation between fasting and nonfasting assessments varied as a function of the variables derived from the questionnaire (age, gender, tobacco use, alcohol use, medication use, or comorbid conditions). In conducting these analyses, scores on the nonfasting assessments were predicted by the fasting assessment, the other predictor variable, and the interaction between the fasting assessment and the other predictor variable. The nonfasting assessment of total cholesterol level, for example, was predicted by the fasting total cholesterol level, age, and the age by fasting total cholesterol measure. Nonsignificant interaction terms from these analyses would support the conclusion that the relation between the nonfasting and fasting assessment of total cholesterol did not vary as a function of the age of the patient. All of these analyses were conducted for the sample as a whole, then separately for patients who met the screening criteria advocated by the USPSTF and the ACP, which recommend screening for men 35 years of age or older and women 45 years of age or older.

RESULTS

Between August 1, 1997, and March 30, 1998, 72 men and 109 women gave written informed consent to

participate in this study. Mean age (± 1 SE) of the enrollees was 54.5 ± 1.3 years (range, 21–86 years). One hundred thirty-four patients met the age criteria for cholesterol screening advocated by the USPSTF and the ACP. Each patient had blood drawn twice, once when not fasting, and once after a fast of at least 12 hours. Twenty men and 18 women gave fasting specimens first and then nonfasting specimens within the next 7 days. Fifty-two men and 91 women gave nonfasting specimens obtained first and then fasting specimens within the next 7 days. Review of prior food intake documented by patients before each blood draw verified the appropriate fasting or nonfasting status for each analysis. Analyses indicated that the order of specimens and time between blood draws (mean, 3.35 days; range, 0–7 days) had no influence on the results.

Fasting and Nonfasting Cholesterol Concentrations

Total and HDL cholesterol concentrations under fasting and nonfasting conditions were determined for all 181 patients (Table 1). Concentrations are provided in both the conventional measure of milligrams per deciliter and in SI units of millimoles per liter, using the conversion factor 0.0259. For the sample as a whole, there was a small but significant increase of 3.7 mg/dL or 0.1 mmol/L in total cholesterol ($P < .01$) under nonfasting compared with fasting conditions, although the 2 measures were found to be highly correlated ($P < .001$). The HDL cholesterol concentrations in the two groups were similar. Results were very similar when the analyses were performed for individuals who met the age criteria for screening of the USPSTF and the ACP (Table 1).

Classification of Cholesterol Status

Table 2 shows that for the sample as a whole, the proportion of patients classified as high in total cholesterol was greater by the nonfasting assessment (46 of 181) than by the fasting assessment (33 of 181). Overall, fasting and nonfasting assessments agreed on classification for 89.5% (162 of 181) of these patients. Coefficient κ was .70 (SE = .06; $P < .001$). The sensitivity and specificity of the nonfasting assessment were 90.9% (95% CI, 85.5% to 94.5%) and 89.2% (95% CI, 83.5% to 93.2%), respectively. The results were very similar when the analysis was restricted to patients who met the age criteria for screening of the USPSTF and the ACP. Compared with the fasting assessment, the nonfasting assessment classified a greater proportion of patients as high in total cholesterol (40 vs 29 of 134; Table 2). The fasting and nonfasting assessments agreed on the classification for 87.3% (117 of 134) of these patients. Coefficient κ was .67 (SE = .07; $P < .001$). The sensitivity and specificity of the nonfasting assessment relative to the fasting assessment were 89.7% (95% CI, 83.0% to 94.1%) and 86.7% (95% CI, 79.6% to 91.7%), respectively.

For the sample as a whole, the fasting assessment identified a higher proportion of patients (83 vs 75 of 181) as having desirable levels of total cholesterol than the nonfasting assessment (Table 2). The two assessments agreed on the classification for 86.7% (157 of 181) of these patients. Coefficient κ was .73 (SE = .10; $P < .001$). Sensitivity and specificity of the nonfasting assessment were 78.8% (95% CI, 72.0% to 84.4%) and 91.8% (95% CI, 86.6% to 95.2%), respectively. Once again, the results were very similar when the analysis was restricted to patients who met the age criteria for screening of the USPSTF and the ACP. Compared with the fasting assessment, the nonfasting assessment classified a smaller proportion of patients as having desirable levels of total cholesterol (45 vs 50 of 134; Table 2). The fasting and nonfasting assessments agreed on the classification for 85.8% (115 of 134) of these patients. Coefficient κ was .69 (SE = .07; $P < .001$). The sensitivity and specificity of the nonfasting assessment relative to the fasting assessment were 76.0% (95% CI, 67.7% to 82.8%) and 91.7% (95% CI, 85.6% to 94.2%), respectively.

Table 1. Comparison of Results for Non-fasting and Fasting Conditions

Measure	Fasting, mg/dL (mmol/L) ± 1 SE [Range, mg/dL]	Nonfasting, mg/dL (mmol/L) ± 1 SE [Range, mg/dL]	Intraclass Correlation (95% Confidence Interval)
All patients			
Total cholesterol	205.2 (5.31) ± 2.7 [110 to 317]	208.9 (5.41) ± 2.8* [123 to 318]	.92† (.90 to .94)
HDL§ cholesterol	51.5 (1.33) ± 1.0 [25 to 99]	50.7 (1.31) ± 1.1 [23 to 94]	.92† (.89 to .94)
Older patients only‡			
Total cholesterol	211.9 (5.48) ± 3.1 [123 to 317]	215.9 (5.59) ± 3.1* [136 to 318]	.90† (.86 to .93)
HDL§ cholesterol	50.6 (1.31) ± 1.3 [25 to 99]	49.3 (1.28) ± 1.2* [23 to 94]	.92† (.89 to .95)

*$P < .01$, compared with fasting value.
†$P < .001$.
‡Men aged 35 years or older and women aged 45 years or older.
§HDL indicates high-density lipoprotein.

Table 2. Identification of Patients with High Total Cholesterol, Desirable Total Cholesterol, and Low High-Density Lipoprotein (HDL) Cholesterol Levels Using Nonfasting and Fasting Assessments

	High Total Cholesterol (≥240 mg/dL [6.22 mmol/L])			Desirable Total Cholesterol (<200 mg/dL [5.18 mmol/L])			Low HDL Cholesterol (<35 mg/dL [0.91 mmol/L])		
	Nonfasting,	Fasting		Nonfasting,	Fasting		Nonfasting,	Fasting	
Patient Group	mg/dL	≥240 mg/dL	<240 mg/dL	mg/dL	<200 mg/dL	≥200 mg/dL	mg/dL	<35 mg/dL	≥35 mg/dL
All patients	≥240	30	16	<200	67	8	<35	12	10
All patients	<240	3	132	≥200	16	90	≥35	6	153
Older patients*	≥240	26	14	<200	38	7	<35	11	9
Older patients	<240	3	91	≥200	12	77	≥35	5	109

*Men aged 35 years or older and women aged 45 years or older.

For the sample as a whole, the nonfasting assessment identified a slightly higher proportion of patients (22 vs 18 of 181) as having low levels of HDL cholesterol compared with the fasting assessment (Table 2). The 2 assessments agreed on the classification for 91.2% (165 of 181) of these patients. Coefficient κ was .55 (SE = .10; $P < .001$). Sensitivity and specificity of the nonfasting assessment were 66.7% (95% CI, 62.1% to 73.4%) and 93.9% (95% CI, 89.4% to 96.7%), respectively. When the analysis was restricted to patients who met the age criteria for screening of the USPSTF and the ACP, the nonfasting assessment classified a greater proportion of patients as having low levels of HDL cholesterol (20 vs 16 of 134; Table 2). The fasting and nonfasting assessments agreed on the classification for 89.6% (120 of 134) of these patients. Coefficient κ was .55 (SE = .11; $P < .001$). The sensitivity and specificity of the nonfasting assessment relative to the fasting assessment were 68.8% (95% CI, 60.1% to 76.4%) and 92.4% (95% CI, 86.2% to 96.1%), respectively.

Finally, the fasting and nonfasting assessments identified similar proportions of patients with borderline-high levels of total cholesterol (7 vs 6 of 60) as having a low level of HDL cholesterol for the sample as a whole (Table 3). The two assessments agreed on the classification for 95.0% (57 of 60) of these patients. Coefficient κ was .74 (SE = .14; $P < .001$). Sensitivity and specificity of the nonfasting assessment were 83.3% (95% CI, 71.0% to 88.3%) and 96.3% (95% CI, 88.2% to 98.4%), respectively.

Table 3. Identification of Patients with Low Levels of High-Density Lipoprotein Cholesterol (<35 mg/dL [0.91 mmol/L]) Using Nonfasting and Fasting Assessments in Patients with Total Cholesterol from 200 to 239 mg/dL (5.18 to 6.22 mmol/L)

	Nonfasting,	Fasting	
Patient Group	mg/dL	<35 mg/dL	≥35 mg/dL
All patients	<35	5	2
All patients	≥35	1	52
Older patients*	<35	5	2
Older patients	≥35	1	41

*Men aged 35 years or older and women aged 45 years or older.

The results were very similar when the analysis was restricted to patients who met the age criteria for screening of the USPSTF and the ACP. Once again, the nonfasting and fasting assessments identified similar proportions of patients with borderline-high levels of total cholesterol (7 vs 6 of 49) as having a low level of HDL cholesterol (Table 3). The two assessments agreed on the classification for 93.9% (46 of 49) of these patients. Coefficient κ was .73 (SE = .15; $P < .001$). Sensitivity and specificity of the nonfasting assessment relative to the fasting assessment were 83.3% (95% CI, 69.4% to 91.9%) and 95% (95% CI, 91.9% to 97.7%), respectively.

Regression Analyses

None of the interaction terms for any of the variables derived from the questionnaire (age, gender, tobacco use, alcohol use, medication use, or comorbid conditions) were found to be significant. Thus, the relation between the nonfasting and fasting assessments for total cholesterol did not vary as a result of any characteristics of the patients examined.

DISCUSSION

There are two major findings of the study. First, there were statistically significant differences in total cholesterol results between the fasting and nonfasting state, but no significant difference between fasting and nonfasting HDL cholesterol results. Total cholesterol values were slightly higher in the nonfasting state, but fasting and nonfasting values were highly correlated. Age, gender, medication use, alcohol use, tobacco use, or the presence of comorbid medical conditions did not influence the difference between fasting and nonfasting total cholesterol values.

Second, this study demonstrates that nonfasting blood screening can accurately classify patients over the age of 20 years into risk groups to guide decisions about primary prevention of coronary heart disease. The agreement between nonfasting and fasting blood testing in classification of patients into desirable cholesterol and

high-cholesterol groups was 86.7% and 89.5%, respectively. For the borderline-high cholesterol group, for whom levels of HDL cholesterol are important in determining subsequent management, there was 95% agreement between fasting and nonfasting HDL cholesterol results. Only a fraction of those patients for whom classification differed were placed in a lower-risk group on the basis of nonfasting assessments. In these few patients, there is the potential for less-rigorous monitoring and treatment of their cholesterol status. These findings were confirmed in this study also for the subgroups of men aged 35 years and older and women aged 45 years and older.

The results of this study are similar to those of previous investigations performed in controlled laboratory settings.[6–11] Our data therefore support the recommendations of the ATP II expert panel that screening adults aged 20 years and older,[1,2] and the USPSTF and ACP recommendations that screening men aged 35 years and older and women aged 45 years and older,[3,4] every 5 years for cholesterol in the nonfasting state provides accurate results to guide physicians in their decisions about primary prevention of coronary heart disease. The advantage of screening on a nonfasting basis is that it allows physicians to screen individuals for cholesterol level at the time they are seen for other primary complaints without requiring them to return after the minimum 12-hour fast.

One limitation of this study is that no information was formally recorded about patients who declined to participate in the study. Our impression is that less than 5% of the patients declined participation, and the primary reason these patients declined was an unwillingness to return within 7 days for the required second blood sampling.

In 1998, the National Cholesterol Education Program released an update summarizing progress and prospects for improving cholesterol screening and primary prevention of coronary heart disease in this country.[13] The progress report acknowledged increasing physician and public awareness of the importance of measuring and treating high cholesterol and primary prevention of coronary heart disease. The report reinforced ATP II guidelines that total and HDL cholesterol can be measured on a nonfasting basis and should be checked in all adults aged 20 years or older at least once every 5 years.[1,2] The present study conducted in a typical clinical practice strengthens these recommendations.

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