Background: Although current guidelines recommend measuring lipid levels in a fasting state, recent studies suggest that nonfasting lipid profiles change minimally in response to food intake and may be superior to fasting levels in predicting adverse cardiovascular outcomes. The objective of this study was to investigate the association between fasting times and lipid levels.

Methods: Cross-sectional examination of laboratory data, including fasting duration (in hours) and lipid results, was performed over a 6-month period in 2011 in a large community-based cohort. Data were obtained from Calgary Laboratory Services, Calgary, Alberta, Canada, the sole supplier of laboratory services for Calgary and surrounding areas (source population, 1.4 million persons). The main outcome measures were mean levels of high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, total cholesterol, and triglycerides for fasting intervals from 1 hour to more than 16 hours. After differences in individual ages were controlled for, linear regression models were used to estimate the mean levels of cholesterol subclasses at different fasting times.

Results: A total of 209,180 individuals (111,048 females and 98,132 males) were included in the study. The mean levels of total cholesterol and high-density lipoprotein cholesterol differed little among individuals with various fasting times. The mean calculated low-density lipoprotein cholesterol levels showed slightly greater variations of up to 10% among groups of patients with different fasting intervals, and the mean triglyceride levels showed variations of up to 20%.

Conclusion: Fasting times showed little association with lipid subclass levels in a community-based population, which suggests that fasting for routine lipid levels is largely unnecessary.


Current guidelines recommend that total lipids and lipid subclass levels be measured with the patient in a fasting state (>8 hours after the last meal).¹² Fasting recommendations were originally introduced to decrease variability and achieve consistency in the metabolic states of patients at the time of sample collection.³ Several studies, however, suggest that the measurement of lipid subclasses in a nonfasting state is an acceptable alternative,⁴ with some nonfasting markers being better at predicting the risk of cardiac events.⁵⁶ Studies suggest that lipid levels vary relatively little between the fasting and the nonfasting states⁷ and that the risk of coronary heart disease and strokes is similarly increased for both nonfasting and fasting lipid levels. Furthermore, as humans are usually in a nonfasting state,⁸ nonfasting values may be more representative of usual metabolic conditions.¹ Measurement of nonfasting lipid profiles may also be better able to reveal individual metabolic abnormalities in lipid clearance, which may ultimately better predict cardiovascular disease risk.⁹ With the exception of the Copenhagen General Population Study and the Copenhagen Heart Study, prior studies were limited by being restricted to selected patients rather than including population-level estimates of the effect of fasting on lipid levels. Therefore, there was a need for a large-scale study of the association of fasting time with lipid levels in an unselected population.

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The purpose of this study was to investigate the association of fasting duration (in hours) with lipid levels in a large...
community-based population. We hypothesized that lipid levels would not vary significantly with duration of fasting time.

METHODS

This study was conducted using secondary data from the laboratory information system at Calgary Laboratory Services (CLS). Calgary Laboratory Services is the sole supplier of laboratory services for Calgary, Alberta, Canada, reporting 23,000,000 tests per year for a population of approximately 1.4 million persons. Approximately 99% of cholesterol tests processed by CLS are performed on community-based individuals, and the remaining 1% are performed on hospital-based patients. A policy change in early 2011 permitted the laboratory to process patient samples for fasting lipid levels irrespective of the duration of the fasting time. With this policy change, the duration of fasting time (in hours) was required to be recorded and included in the laboratory report, permitting the capture of both lipid levels and fasting intervals. For the 6-month period from April 1, 2011, to September 30, 2011, we examined the test results of all individuals with lipid test panels (high-density lipoprotein [HDL] cholesterol, low-density lipoprotein [LDL] cholesterol, total cholesterol, and triglycerides) performed by CLS. For patients with multiple measurements, only the first lipid test panel during the 6-month period was included.

All testing was performed at CLS using standard laboratory protocols on modular analyzers (Roche). High-density lipoprotein cholesterol and triglyceride levels were measured directly; LDL cholesterol levels were estimated using the Friedewald equation. Time since last meal (fasting duration, in hours) was obtained by self-report from the patient at the time of testing. For the purpose of analysis, fasting time was stratified into hourly intervals from 0 to 16; fasting times longer than 16 hours were included in the 16-hour category. The 1-hour category included individuals who had fasted for less than 1 hour. Records with missing data for time since last meal were excluded. For individuals with triglyceride levels greater than 400 mg/dL (to convert to millimoles per liter, multiply by 0.0113), the calculated LDL level was not reported, and the LDL values for those individuals were therefore not included in our analyses. Age was categorized into 5-year intervals following the methodology of Langsted et al. Individuals older than 80 years were categorized into 1 group.

Previous work has shown that fasting time varies as a function of age and sex. To control for these effects, we analyzed data for males and females separately. For each sex, we constructed linear regression models (SPSS general linear models) with cholesterol measurements as the dependent variable and fasting time (in hours) and age (in 5-year cohorts) as independent variables. In these models, both age and fasting time were significant predictors of cholesterol level and also showed significant interactions. We then calculated estimated marginal means with 95% confidence intervals for each lipid component at each fasting time period, with age held constant at the group mean. We assessed statistical significance by comparing mean cholesterol subgroup measurements obtained at 9 to 12 hours (criteria used in the Adult Treatment Panel III study) and at more than 8 hours (criteria used in the Copenhagen General Population and Copenhagen Heart Study studies) with all other fasting time intervals. In these comparisons, the Scheffé post hoc test was used to control for the effects of multiple pairwise testing. Statistical analyses were performed using SPSS version 19.0 for Windows. The study was approved by the University of Calgary institutional ethics review board.

RESULTS

A total of 213,433 individuals had at least 1 lipid profile completed during the study period. After records with missing fasting times were excluded (n=4,253), a total of 209,180 individuals were included in the analyses. Their baseline characteristics are shown below (to convert cholesterol values to millimoles per liter, multiply by 0.0259):

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (range), y</td>
<td>05.8 (0-103)</td>
</tr>
<tr>
<td>Females, No. (%)</td>
<td>111,052 (53.1)</td>
</tr>
<tr>
<td>Males, No. (%)</td>
<td>98,132 (46.9)</td>
</tr>
<tr>
<td>Total cholesterol, mean (SD), mg/dL</td>
<td>183.4 (40.3)</td>
</tr>
<tr>
<td>HDL cholesterol, mean (SD), mg/dL</td>
<td>55.2 (16.3)</td>
</tr>
<tr>
<td>Calculated LDL cholesterol, mean (SD), mg/dL</td>
<td>103.3 (34.3)</td>
</tr>
<tr>
<td>Triglycerides, mean (SD), mg/dL</td>
<td>127.6 (101.8)</td>
</tr>
</tbody>
</table>

The estimated mean cholesterol subclass levels by fasting time are shown in Table 1 (males) and Table 2 (females). In general, the mean cholesterol subclass levels varied by less than 2% for total cholesterol and HDL cholesterol, by less than 10% for calculated LDL cholesterol, and by less than 20% for triglycerides. Statistically significant differences among cholesterol subclass levels were present only for a minority of fasting intervals when compared with either a 9- to 12-hour fasting time or a greater than 8-hour fasting time.

COMMENT

We found that fasting time showed little association with lipid subclass levels in a large community-based cohort. This finding suggests that fasting for routine lipid level determinations is largely unnecessary. Our study corroborates the findings of previous smaller studies. Further data on this question are important for several reasons. First, fasting for routine blood work presents an inconvenience for patients and may discourage compliance with routine screening programs. Second, because fasting blood work is generally performed in the morning, the large number of phlebotomies performed for screening lipid testing may create increased wait times at phlebotomy clinics, which may further inconvenience patients and decrease compliance with screening. Previous work has shown that peak triglyceride levels measured 4 hours after meals yield the strongest predictive relationship of cardiovascular events. Also, it has been reported that insulin resistance is associated with worse postprandial lipid or lipoprotein clearance and that increased postprandial triglyceride levels and decreased HDL cholesterol levels are excellent predictors of insulin resistance, a key metabolic abnormality in type 2 diabetes. These findings suggest that analysis of fasting time and lipid levels could have a role in identifying individuals for further screening with supplementary tests such as oral triglyceride tolerance testing or more rigorous treatment protocol goals and closer monitoring. The elimination of a fasting requirement for lipid determination could also increase patient compliance with testing, which could have particular benefits for patients with diabetes, many of whom have difficulty with prolonged fasting.
ease have been nearly identical in meta-analyses.10 Third, lipid and apolipoproteins in predicting cardiovascular diseases are not always directly comparable, and they may differ from other risk markers such as the apolipoprotein B-100, apolipoprotein A-1, or apolipoprotein B-100 levels.9

However, it should also be noted that recent comparisons of hazard ratios between individual meal choices before blood draws were not examined, and we could not control for recall errors for self-reported fasting times. Second, our clinical data were limited to measurements commonly taken as part of screening blood work and did not include apolipoprotein B-100, apolipoprotein A-1, or apolipoprotein B-100 levels.9 Therefore, we could not comment on the predictive value of fasting vs nonfasting levels on cardiovascular outcomes owing to a lack of patient outcome data. Fourth, we did not have knowledge of pharmacological treatment of individual subjects, although a previous study reported that patients who were taking lipid-lowering drugs did not differ from controls in regard to changes in nonfasting vs fasting lipid subclass levels. Fifth, because we used secondary data on all individuals presenting for cholesterol testing rather than a random sample of individuals drawn from the general population, our findings should be interpreted with caution.

There are several limitations to this study. First, individual meal choices before blood draws were not examined, and we could not control for recall errors for self-reported fasting times. Second, our clinical data were limited to measurements commonly taken as part of screening blood work and did not include apolipoprotein B-100, apolipoprotein A-1, or apolipoprotein B-100 levels.9 However, it should also be noted that recent comparisons of hazard ratios between lipid and apolipoproteins in predicting cardiovascular disease have been nearly identical in meta-analyses.10 Third, we could not comment on the predictive value of fasting vs nonfasting levels on cardiovascular outcomes owing to a lack of patient outcome data. Fourth, we did not have knowledge of pharmacological treatment of individual subjects, although a previous study reported that patients who were taking lipid-lowering drugs did not differ from controls in regard to changes in nonfasting vs fasting lipid subclass levels. Fifth, because we used secondary data on all individuals presenting for cholesterol testing rather than a random sample of individuals drawn from the general population, our findings should be interpreted with caution.
Fasting for Lipid Testing

Is It Worth the Trouble?

Lipid testing plays a major role in cardiovascular risk stratification and the assessment of lipid responses to clinical interventions. Current guidelines suggest that blood samples for lipid profiles should be obtained after a 9- to 12-hour fast. This requirement is not always practical for patients, who rarely present to health care providers in a fasting state. Patients often expend additional resources to return to a laboratory while interpreted as representative of individuals presenting for screening and therefore may represent a biased sample of the general population. Furthermore, we cannot exclude the possibility that individuals with specific medical conditions (for example diabetes or dyslipidemia) may have been more or less likely to have been compliant with the recommendation to fast before cholesterol testing. Finally, our laboratory did not calculate LDL cholesterol levels when triglyceride levels were higher than 400 mg/dL, which excluded the analysis of LDL cholesterol levels on 1.5% of our study population. The results presented herein, combined with those of other recent studies, suggest that nonfasting determination of lipid subclasses is a reasonable alternative to fasting determinations. In individuals with an initial triglyceride level higher than 400 mg/dL, follow-up assessment of fasting lipid levels and/or direct measurement of LDL cholesterol levels could be considered. A possible future direction will be to address this question more directly by examining repeated measurements with differing fasting times in the same individuals.

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Author Contributions: Dr Naugler had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Sidhu and Naugler. Acquisition of data: Sidhu and Naugler. Analysis and interpretation of data: Sidhu and Naugler. Drafting of the manuscript: Sidhu and Naugler. Critical revision of the manuscript for important intellectual content: Sidhu and Naugler. Statistical analysis: Sidhu and Naugler. Administrative, technical, and material support: Sidhu and Naugler. Study supervision: Naugler.

Conflict of Interest Disclosures: None reported.

REFERENCES


