Nonfasting Lipids, Lipoproteins, and Apolipoproteins in Individuals with and without Diabetes: 58 434 Individuals from the Copenhagen General Population Study

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BACKGROUND: Whether lipid profiles should be collected from fasting or nonfasting individuals is controversial, particularly in the diabetic population. We examined the influence of normal food intake on lipid profiles in diabetic and nondiabetic individuals.

METHODS: We assessed plasma concentrations of lipids, lipoproteins, apolipoproteins, and albumin as a function of time since the last meal in 58 434 individuals (participation rate 45%) from the general population, 2270 of whom had diabetes mellitus.

RESULTS: Similar patterns in the measured constituents were observed in the diabetic and nondiabetic populations. Triglycerides remained increased for 6–7 h in both populations after the last meal, whereas LDL cholesterol and albumin but not apolipoprotein B were reduced in both populations up to 5 h after normal food intake; after adjustment for hemodilution on the basis of albumin concentrations, the LDL cholesterol reductions were no longer present. Maximum observed mean differences from fasting concentrations in diabetic patients were −0.6 mmol/L, 0 mmol/L, 0.2 mmol/L, and 0.08 g/L (8 mg/dL) for LDL cholesterol, HDL cholesterol, triglycerides, and apolipoprotein B, respectively, and, correspondingly, −0.3 mmol/L, 0 mmol/L, 0.2 mmol/L, and 0.03 g/L (3 mg/dL) in individuals without diabetes.

CONCLUSIONS: Triglycerides increased up to 0.2 mmol/L after normal food intake in individuals with and without diabetes, whereas the postprandial reductions in LDL cholesterol observed in both populations likely were caused by hemodilution due to fluid intake. No statistically significant differences in postprandial apolipoprotein B concentrations were found. These data may be useful for discussion during revisions of guidelines for lipid measurements in individuals with or without diabetes.

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Whether lipid profiles should be measured in the fasting or nonfasting state is a controversial issue, particularly in individuals with diabetes, who often have high triglycerides, the lipid fraction most affected by food intake. Lipids, lipoproteins, and apolipoproteins are conventionally measured in the fasting state for cardiovascular risk prediction, that is, at least 8 h after the last meal (1–3). However, after normal food intake, concentrations of lipids, lipoproteins, and apolipoproteins differ only minimally from the fasting to the nonfasting state in the average person in the general population (4,5). Whether this observation holds both for individuals with and without diabetes is presently unknown. Measurements of lipids, lipoproteins, and apolipoproteins in either the fasting or nonfasting state can be used for cardiovascular risk prediction (4, 6), whereas nonfasting triglycerides as a marker of increased remnant cholesterol appear to be better for predicting risk of myocardial infarction, ischemic stroke, and early death (7–9).

Diabetic patients have a higher risk of atherosclerotic cardiovascular disease than nondiabetic patients (2,3). Lipid derangements in diabetes are important contributors to this higher risk and consist mainly of increases in plasma triglycerides and decreases in HDL cholesterol combined with sufficiently high concentrations of LDL cholesterol to cause atherosclerosis (10–12). Owing to the commonly observed increases in triglycerides in diabetes, it is possible that excessive postprandial lipemia in particular may contribute substantially to atherosclerotic cardiovascular disease in diabetes (13–16). However, postprandial lipemia may be masked when lipid profiles are measured in individ-

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uals in the fasting state, and therefore fasting measurements may not be optimal for evaluating cardiovascular risk in individuals with diabetes.

We examined the influence of normal food intake on the concentrations of lipids, lipoproteins, and apolipoproteins in individuals with and without diabetes. We conducted this study in 58 434 patients from the Copenhagen General Population Study, of whom 2270 suffered from diabetes mellitus. All participants were examined with a full lipid profile measured in a single laboratory by using the same methods throughout 6 years of recruitment.

Materials and Methods

PARTICIPANTS WITH AND WITHOUT DIABETES

Participants from the Copenhagen General Population Study (8, 17, 18) were recruited randomly from the general population of Copenhagen by using the Danish Central Person Registration number, which uniquely identifies all individuals living in Denmark. All participants were white and of Danish descent. This study was approved by a Danish ethics committee (#H-KF-01-144/01) and by Herlev Hospital, Copenhagen University Hospital. The study was conducted according to the Declaration of Helsinki, and all participants gave written informed consent.

Of individuals invited to the Copenhagen General Population Study and thus to a free health examination, 45% participated. Before attending, participants filled out a questionnaire on medical history and use of medication. The participants then went to the Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, where a health examiner checked the questionnaire and the participant could ask clarifying questions. Also, a physical examination was performed; body mass index (BMI) was measured as weight divided by measured height squared (kg/m^2). Furthermore, a blood sample was taken to determine plasma concentrations of glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, and albumin. Finally, participants were asked the time of their last meal at the time of blood sampling. The times of last food intake were categorized as 0–1, 1–2, 2–3, 3–4, 4–5, 5–6, 6–7, 7–8, or >8 h ago.

In this study, we examined the first 58 434 individuals in the Copenhagen General Population Study, examined in 2003–2009. Of these individuals, 2270 individuals had diabetes mellitus at the time of blood sampling. We defined a person with diabetes mellitus as a person with self-reported diabetes, a person taking insulin or other antidiabetic medication, and/or a person with a random plasma glucose >11 mmol/L. We do not have any knowledge of whether individuals with diabetes suffered from type 1 or type 2 diabetes. However, because most participants with diabetes were older [median age 66 years (interquartile range 59–73 years)], it is likely that primarily type 2 diabetes mellitus was represented in this population.

ANALYSES

Standard hospital assays (Konelab) performed at the Department of Clinical Biochemistry, Herlev Hospital, Copenhagen University Hospital, were used on fresh blood samples to measure plasma concentrations of glucose, total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides, apolipoprotein A1, apolipoprotein B, and albumin. Non-HDL cholesterol was calculated as total cholesterol minus HDL cholesterol. If triglycerides were <4 mmol/L, LDL cholesterol was calculated by the Friedewald equation; otherwise, LDL cholesterol was measured directly. All assays were followed daily for precision by using internal controls and 4–12 times yearly for accuracy with a Scandinavian external QC program.

STATISTICAL ANALYSES

All statistical analyses were carried out by using Stata 10 (Stata Corp). Power calculations were performed by using National Council for the Social Studies Power Analysis and Sample Size software. We used general linear models to adjust for age and sex; for age, sex, and lipid-lowering therapy; and for age, sex, and plasma albumin concentrations. Because sex distribution differed as a function of time since the last meal, men and women were stratified into age groups of 5 years from the age of 20 to >80 years in these analyses. Student t-tests were used to identify differences in concentrations of lipids, lipoproteins, apolipoproteins, and albumin as a function of time since the last meal: differences were tested between >8 h since the last meal (fasting) and the 8 other time points (0–1, 1–2, 2–3, 3–4, 4–5, 5–6, 6–7, and 7–8 h since the last meal). All t-tests were corrected for multiple comparisons with the Bonferroni method (that is, all P values were multiplied by the number of parallel tests) (19). We had 80% statistical power at 2-sided $P < 0.05$ to detect increases in triglycerides at 0–1, 1–2, 2–3, 3–4, 4–5, 5–6, 6–7, and 7–8 h vs fasting of 0.1, 0.1, 0.1, 0.1, 0.1, 0.1, 0.2, and 0.2 mmol/L in individuals without diabetes, respectively, and of 0.5, 0.5, 0.5, 0.5, 0.5, 0.6, 0.8, and 0.9 mmol/L in individuals with diabetes, respectively. Corresponding values for apolipoprotein B were 4, 4, 4, 4, 4, 4, 5, and 6 mg/dL in individuals without diabetes, respectively, and 17, 16, 16, 16, 17, 18, 24, and 26 mg/dL in individuals with diabetes, respectively.

Results

Table 1 shows characteristics of the individuals from the Danish general population, the Copenhagen General

Table 1. Characteristics of individuals from the general population with and without diabetes.[a]

Characteristics	With diabetes	Without diabetes
n	2270	56 164
Men, %	45	44
Age, years	66 (59–73)	57 (47–66)
Total cholesterol, mmol/L	4.9 (4.1–5.6)	5.6 (4.9–6.3)
Non-HDL cholesterol, mmol/L	3.3 (2.6–4.2)	3.9 (3.2–4.7)
LDL cholesterol, mmol/L	2.4 (1.8–3.2)	3.2 (2.6–3.9)
HDL cholesterol, mmol/L	1.4 (1.1–1.7)	1.6 (1.3–2.0)
Triglycerides, mmol/L	1.8 (1.2–2.8)	1.4 (1.0–2.1)
Apolipoprotein A1, mg/dL	149 (132–169)	157 (139–177)
Apolipoprotein B, mg/dL	102 (82–129)	107 (88–130)
Total cholesterol/HDL cholesterol	3.5 (2.7–4.6)	3.5 (2.8–4.5)
Apolipoprotein B/ apolipoprotein A1	0.7 (0.5–0.9)	0.7 (0.5–0.9)
Albumin, μmol/L	595 (561–629)	600 (566–636)
Lipid-lowering therapy, %	52	8
BMI, kg/m^2	29 (26–32)	26 (23–28)

[a] Continuous variables are shown as median (interquartile range). To convert mg/dL to g/L, multiply by 0.01.

Population Study. Of the 58 434 total participants, 2270 individuals (3.9%) had diabetes mellitus at the time of blood sampling.

Median [interquartile range (IQR)] plasma concentration of triglycerides in diabetic individuals was 1.8 (1.2–2.8) mmol/L and 1.4 (1.0–2.1) mmol/L in nondiabetic individuals (Table 1). The corresponding values for HDL cholesterol were 1.4 (1.1–1.7) and 1.6 (1.3–2.0) mmol/L in diabetic and nondiabetic individuals. LDL cholesterol was 2.4 (1.8–3.2) mmol/L in diabetic individuals compared with 3.2 (2.6–3.9) mmol/L in nondiabetic individuals, largely reflecting that 52% of diabetic individuals were taking statins, whereas only 8% of nondiabetic individuals were on statins. For apolipoprotein B, the concentrations were 1.02 (0.82–1.29) g/L [102 (82–129) mg/dL] in diabetic individuals and 1.07 (0.88–1.3) g/L [107 (88–130) mg/dL] in nondiabetic individuals.
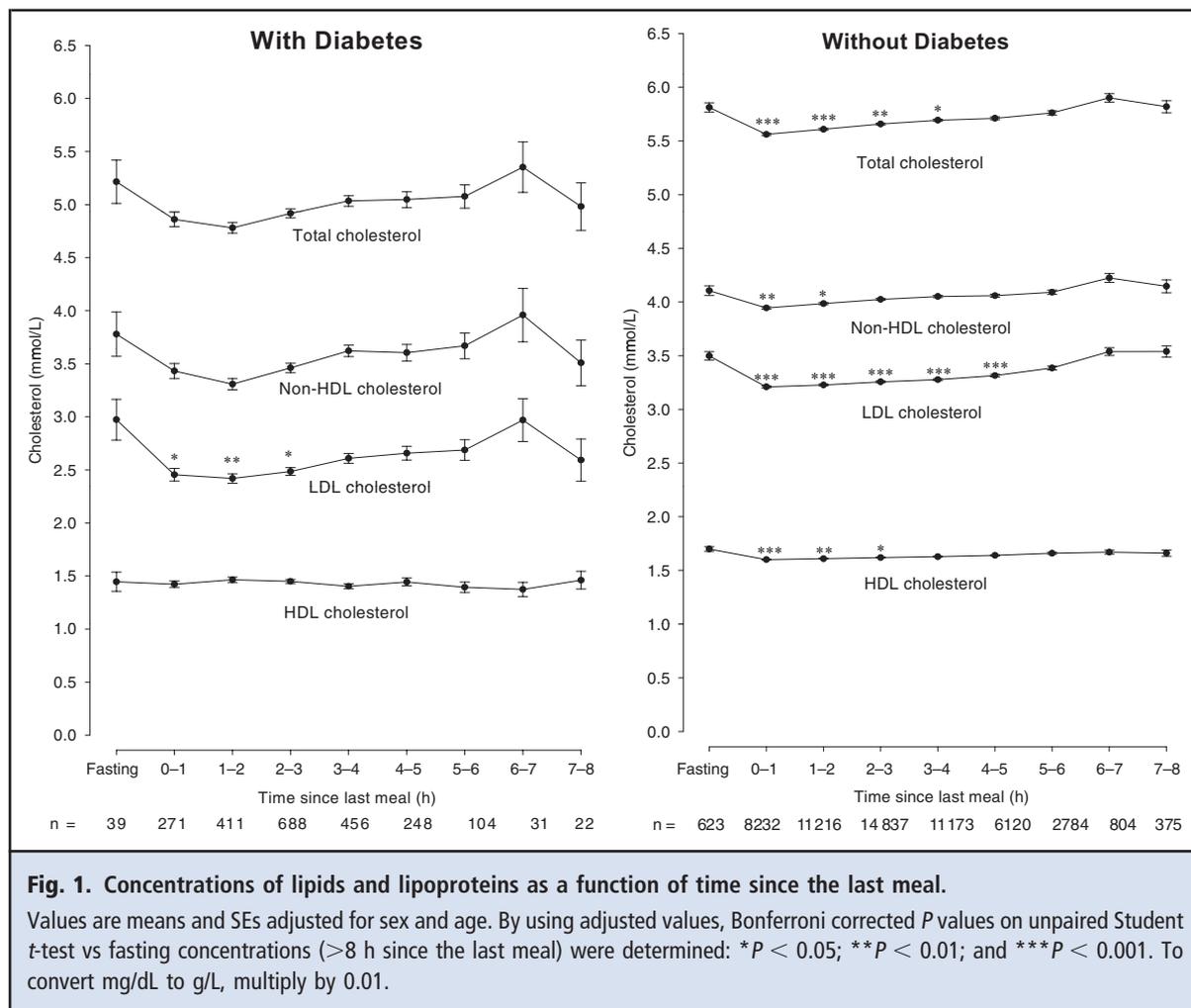
Plasma concentrations of lipids, lipoproteins, apolipoproteins, and albumin as a function of time since the last meal followed similar patterns in individuals with and without diabetes (Figs. 1 and 2); however, because of higher statistical power owing to the higher number of individuals in the nondiabetic vs diabetic groups (56 164 vs 2270 individuals, respectively), more differences compared with fasting concentrations (>8 h since last meal) were found to be significant in the nondiabetic than in the

diabetic individuals. Our reported results were all adjusted only for age and sex; however, similar results were observed when we additionally adjusted for lipid-lowering therapy (data not shown).

Higher triglycerides were observed up to 6–7 h after the last meal compared with fasting concentrations in the nondiabetic population; a similar pattern was seen in individuals with diabetes (Fig. 2). LDL cholesterol was reduced up to 5 h after normal food intake compared with fasting concentrations in individuals with and without diabetes, although these reductions were statistically significant only up to 3 h after normal food intake in individuals with diabetes (Fig. 1). For total cholesterol, non-HDL cholesterol, and HDL cholesterol, the pattern was similar to that for LDL cholesterol in individuals with and without diabetes, but was found to be statistically significant only in individuals in the nondiabetic population, likely because of the higher statistical power in this group (Fig. 1). Finally, apolipoprotein A1, apolipoprotein B, apolipoprotein B/apolipoprotein A1 ratio, and total cholesterol/HDL cholesterol ratio did not change in response to normal food intake compared with fasting concentrations in either the diabetic or nondiabetic individuals (Fig. 2).

Albumin concentrations were reduced up to 5 h after normal food intake compared with fasting concentrations in individuals with and without diabetes, although this reduction was found to be statistically significant only up to 2 h after the last meal in individuals with diabetes. These changes most likely were caused by fluid intake along with food intake and thereby by hemodilution. Indeed, when the results in Figs. 1 and 2 were adjusted additionally for albumin concentrations as a function of time since the last meal, all significant differences in concentrations of lipids, lipoproteins, and apolipoproteins as a function of time since normal food intake compared with fasting concentrations were no longer present, except the increased triglycerides in individuals without diabetes and with a similar nonsignificant trend in individuals with diabetes (data not shown).

Absolute mean differences in concentrations of plasma lipids, lipoproteins, apolipoproteins, and albumin as a function of time since the last meal compared with fasting concentrations were similar in individuals with and without diabetes (Table 2); however, because of the higher numbers of individuals and higher statistical power in the nondiabetic vs diabetic groups (56 164 vs 2270 individuals, respectively), the SEs for mean differences were smaller in the nondiabetic group than in the diabetic group. All of these results were adjusted only for age and sex; however, similar results were seen when we additionally adjusted for lipid-lowering therapy (data not shown).
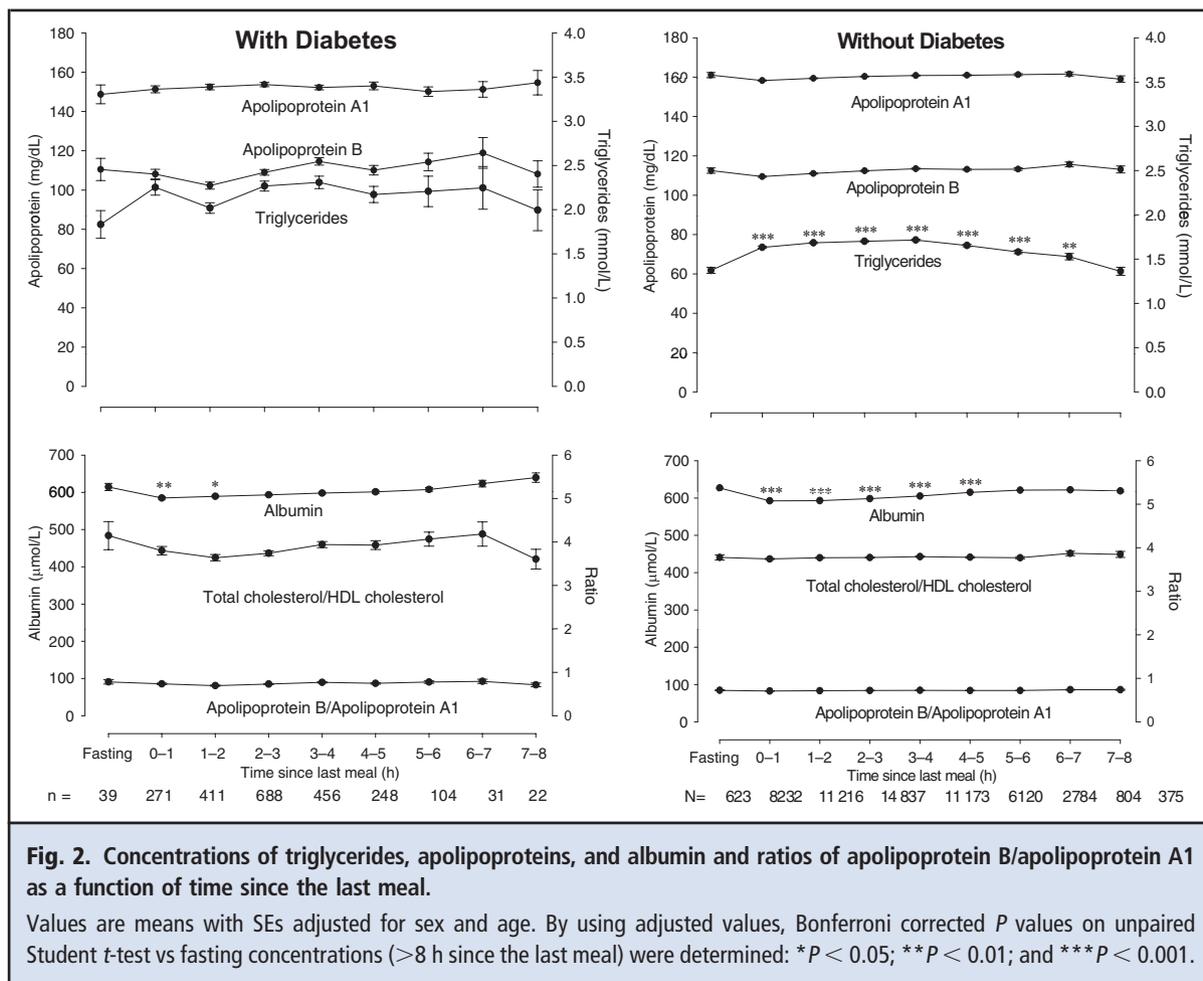
Fig. 1. Concentrations of lipids and lipoproteins as a function of time since the last meal.

Values are means and SEs adjusted for sex and age. By using adjusted values, Bonferroni corrected *P* values on unpaired Student *t*-test vs fasting concentrations (>8 h since the last meal) were determined: *$P < 0.05$; **$P < 0.01$; and ***$P < 0.001$. To convert mg/dL to g/L, multiply by 0.01.

Individuals with diabetes had a maximum mean difference from fasting concentrations of −0.6 mmol/L for LDL cholesterol at 1–2 h after the last meal; 0 mmol/L for HDL cholesterol; 0.2 mmol/L for triglycerides at 0–1, 2–4, and 6–7 h after the last meal; and 8 mg/dL for apolipoprotein B at 6–7 h after the last meal (Table 2, Figs. 1 and 2). The corresponding numbers for individuals without diabetes were −0.3 mmol/L for LDL cholesterol at 0–2 h, 0 mmol/L for HDL cholesterol, 0.2 mmol/L for triglycerides at 0–5 h, and 3 mg/dL for apolipoprotein B at 6–7 h after the last meal.

Discussion

We found that in both the diabetic and nondiabetic groups, plasma triglycerides increased only a maximum of 0.2 mmol/L after normal food intake compared with fasting concentrations. Additionally, we found that reductions in LDL cholesterol after normal food intake in individuals with and without diabetes most likely were

caused by hemodilution due to fluid intake. Apolipoprotein B concentrations did not change after normal food intake, and non-HDL cholesterol also was stable. Because we performed individual studies on 2270 individuals with diabetes and 56 164 without diabetes, all from the general population, these results are novel.

Lipid profiles are conventionally measured in the fasting state *(1–3)*; however, there are advantages to using nonfasting samples rather than fasting samples for lipid profile measurements *(4, 20–22)*. Such advantages led the Danish Society for Clinical Biochemistry in 2009 to recommend that all laboratories in Denmark use random nonfasting lipid measurements as the standard and then offer clinicians the option of remeasurement of triglyceride concentrations in the fasting state only if nonfasting concentrations were >4 mmol/L *(20, 21)*. Because lipid profile measurements often are taken repeatedly in the same patient, a single spurious nonfasting very high triglyceride concentration due to a very high fat intake preceding blood sam-

Fig. 2. Concentrations of triglycerides, apolipoproteins, and albumin and ratios of apolipoprotein B/apolipoprotein A1 as a function of time since the last meal.

Values are means with SEs adjusted for sex and age. By using adjusted values, Bonferroni corrected P values on unpaired Student t-test vs fasting concentrations (>8 h since the last meal) were determined: $*P < 0.05$; $**P < 0.01$; and $***P < 0.001$.

pling will be followed by other measurements with lower concentrations. The most obvious advantage of nonfasting rather than fasting lipid profile measurements is that the blood-sampling process is simplified for patients as well as for general practitioners and hospitals. The experience in Denmark was that this change in blood sampling was easy to implement: after adaptation of the nonfasting strategy by major hospitals in Copenhagen, and subsequent corresponding reports in written and electronic media nationwide, patients in the entire country pushed for similar changes at their local clinical biochemical laboratory.

Lipid experts, however, often put forward several arguments against changing from fasting to nonfasting lipid profiles. First, because triglycerides may increase 1–2 mmol/L after a fat tolerance test *(8, 13, 23)*, there is widespread belief that a similar increase will happen after normal food intake. However, for nonfasting triglycerides taken at random in people in the general population who eat normal meals (as opposed to a fat tolerance test that contains much more fat than most

meals), the variation in triglycerides is indeed modest. In our current investigation of individuals in the Copenhagen General Population Study, we found that plasma triglycerides increased only 0.2 mmol/L after normal food intake in both diabetic and nondiabetic individuals, a finding that is in accord with 2 previous studies in which diabetes status was unknown *(4, 5)*. Furthermore, in the Copenhagen City Heart Study, 6709 individuals without lipid-lowering therapy attended both the baseline 1976–1978 examination and the 1991–1994 examination, 15 years apart; in these individuals, the computed regression dilution ratios for nonfasting triglyceride concentrations were 0.57 for women and 0.60 for men *(9)*. These data suggest that the fluctuation of a nonfasting triglyceride measurement over a span of 15 years in the same individuals is indeed similar to the fluctuation of cholesterol or blood pressure levels. Second, before the availability of direct assays for LDL cholesterol measurement, the estimation of LDL cholesterol was performed almost solely by the use of the Friedewald equation, which officially re-

Table 2. Mean difference in plasma levels of lipids, lipoproteins, and apolipoproteins among nonfasting individuals according to time since the last meal compared with fasting individuals.[a]

Characteristics	Time since last meal, h							
	0–1	1–2	2–3	3–4	4–5	5–6	6–7	7–8
With diabetes, n	271	411	688	456	248	104	31	22
Without diabetes, n	8232	11 216	14 837	11 173	6120	2784	804	375
Total cholesterol, mmol/L								
With diabetes	−0.4 (0.2)	−0.4 (0.2)	−0.3 (0.2)	−0.2 (0.2)	−0.2 (0.2)	−0.1 (0.2)	0.1 (0.3)	−0.2 (0.3)
Without diabetes	−0.3*** (0.0)	−0.2*** (0.0)	−0.2** (0.0)	−0.1* (0.0)	−0.1 (0.0)	0.0 (0.0)	0.1 (0.1)	0.0 (0.1)
Non-HDL cholesterol, mmol/L								
With diabetes	−0.3 (0.2)	−0.5 (0.2)	−0.3 (0.2)	−0.2 (0.2)	−0.2 (0.2)	−0.1 (0.2)	0.2 (0.3)	−0.3 (0.3)
Without diabetes	−0.2** (0.0)	−0.1* (0.0)	−0.1 (0.0)	0.1 (0.0)	0.0 (0.0)	0.0 (0.0)	0.1 (0.1)	0.0 (0.1)
LDL cholesterol, mmol/L								
With diabetes	−0.5* (0.2)	−0.6** (0.2)	−0.5* (0.2)	−0.4 (0.2)	−0.3 (0.2)	−0.3 (0.2)	0.0 (0.3)	−0.4 (0.3)
Without diabetes	−0.3*** (0.0)	−0.3*** (0.0)	−0.2*** (0.0)	0.2*** (0.0)	−0.2*** (0.0)	−0.1 (0.0)	0.0 (0.1)	0.0 (0.1)
HDL cholesterol, mmol/L								
With diabetes	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)
Without diabetes	0.0*** (0.0)	0.0** (0.0)	0.0* (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Triglycerides, mmol/L								
With diabetes	0.2 (0.1)	0.1 (0.1)	0.2 (0.1)	0.2 (0.1)	0.1 (0.1)	0.1 (0.1)	0.2 (0.1)	0.1 (0.1)
Without diabetes	0.2*** (0.0)	0.2*** (0.0)	0.2*** (0.0)	0.2*** (0.0)	0.2*** (0.0)	0.1*** (0.0)	0.1** (0.0)	0.0 (0.0)
Apolipoprotein A1, mg/dL								
With diabetes	2.6 (5.0)	3.7 (4.8)	5.0 (4.8)	3.5 (4.2)	4.3 (5.3)	1.4 (4.9)	2.5 (6.4)	5.9 (7.9)
Without diabetes	−2.8 (1.1)	−1.7 (1.1)	−0.7 (1.1)	−0.2 (1.2)	−0.1 (1.2)	0.2 (1.3)	0.5 (1.6)	−2.1 (2.1)
Apolipoprotein B, mg/dL								
With diabetes	−2.4 (6.9)	−8.3 (6.1)	−1.5 (6.3)	4.1 (6.6)	−0.4 (6.5)	3.8 (8.1)	8.4 (9.4)	−2.3 (9.0)
Without diabetes	−3.1 (1.3)	−1.5 (1.3)	−0.1 (1.3)	1.0 (1.4)	0.6 (1.4)	0.8 (1.5)	3.2 (1.8)	0.6 (2.2)
Albumin, μmol/L								
With diabetes	−30** (8.7)	−25* (8.1)	−21 (8.6)	−16 (8.7)	−13 (10)	−6.7 (10)	9.0 (13)	25 (16)
Without diabetes	−35*** (2.2)	−34*** (2.2)	−29*** (2.1)	−21*** (2.2)	−12*** (2.3)	−5.9 (2.6)	−5.1 (3.0)	−8.2 (3.4)
Apolipoproten B/Apolipoprotein A1								
With diabetes	0.0 (0.1)	−0.1 (0.0)	−0.1 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.1)	0.0 (0.1)	−0.1 (0.1)
Without diabetes	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)	0.0 (0.0)
Total cholesterol/HDL cholesterol								
With diabetes	−0.3 (0.3)	−0.5 (0.3)	−0.4 (0.3)	−0.2 (0.3)	−0.2 (0.3)	−0.1 (0.3)	0.0 (0.4)	−0.5 (0.5)
Without diabetes	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.0 (0.1)	0.1 (0.1)	0.1 (0.1)

[a] Values are mean difference from fasting (SE). Using adjusted values, Bonferroni corrected P values on unpaired Student t-test vs fasting levels (>8 h since the last meal) were as follows: *P <0.05, **P <0.01, and ***P <0.001. To convert mg/dL to g/L, multiply by 0.01.

quires a fasting triglyceride value (1, 24). However, we have shown in the current study that calculated LDL cholesterol concentrations do not change in response to normal food intake in individuals with and without diabetes after correction for hemodilution. In addition, we previously documented that increased nonfasting calculated LDL cholesterol predicts increased risk of cardiovascular events (4), just as well as fasting concentrations. Finally, in the Women's Health Study, measured and calculated LDL cholesterol values were highly correlated, both in fasting individuals (n = 19 777) and in nonfasting individuals (n = 6615) (both Pearson correlation coefficients were >0.97) (25).

Nevertheless, it is still often perceived as controversial whether lipid profiles should be measured in the fasting or nonfasting state, particularly in individuals with diabetes, who often have high triglycerides, the lipid fraction most affected during a fat tolerance test (13, 23). Indeed, one of the problems of diabetic dyslipidemia is excessive postprandial lipemia along with increased plasma triglycerides and low concentrations of HDL cholesterol, derangements that each may contribute to the increased risk of developing atherosclerosis and cardiovascular disease in diabetes (12, 14–16, 26–30). However, the present results clearly demonstrate absence of any excessive postprandial li-

pemia after normal food intake in individuals with diabetes.

Ostensibly, the decrease in LDL cholesterol after normal food intake would seem to be of concern for introducing nonfasting lipid measurements as a standard. However, because we observed a similar decrease in albumin concentrations after normal food intake, and LDL cholesterol concentrations no longer changed after normal food intake after adjustment for albumin concentrations, the explanation for the modestly lower concentrations of LDL cholesterol likely is fluid intake together with food intake, and thus hemodilution. Nevertheless, one could still argue that the lower concentrations of LDL cholesterol after food and fluid intake present a real problem in clinical practice; however, the irony is that many laboratories in Denmark and elsewhere allow patients to drink water, coffee, and/or tea without added milk, sugar, and cream before a lipid profile measurement. This means that even for a conventional fasting lipid profile, many laboratories already have introduced involuntarily the small problem with hemodilution due to fluid intake before blood sampling.

We found that only the concentrations of triglycerides increased after normal food intake compared with fasting concentrations, with only a minimal change of up to 0.2 mmol/L. Because such modest postprandial lipemia may be masked by measuring lipid profiles in the fasting state, fasting concentrations may not be optimal for evaluating cardiovascular risk in individuals with diabetes, particularly because nonfasting triglycerides as a marker of increased remnant cholesterol appear to be particularly good at predicting risk of myocardial infarction, ischemic stroke, and early death in the average person in the general population (7–9).

The changes shown in Table 2 for apolipoprotein B suggest that apolipoprotein B may possibly differ according to fasting status, especially among individuals with diabetes, with the lowest mean difference being −8 mg/dL and the highest being 8 mg/dL depending on time since the last meal. Although these differences were not found to be statistically significant among individuals with diabetes, the values fluctuated much more according to nonfasting status than in nondiabetic individuals. This difference in observed fluctuation of apolipoprotein B between individuals with and without diabetes most likely is attributable to higher statistical power in the nondiabetic vs diabetic populations we studied (56 164 vs 2270 individuals, respectively). In the nondiabetic population, apolipoprotein B concentrations did not change after normal food intake and non-HDL cholesterol also was quite stable.

There are only a few smaller studies that have examined the association between nonfasting/postprandial concentrations of lipids, lipoproteins, and apolipoproteins and risk of cardiovascular disease se-

lectively in individuals with diabetes, and these studies showed conflicting results (31–35). Teno et al. (31) found among 60 patients with diabetes mellitus that there was a correlation between increased concentrations of postprandial triglycerides and increased carotid intima media thickness; this finding was more significant for concentrations of nonfasting triglycerides than for fasting triglycerides. Also, Carstensen et al. (32) showed that nonfasting triglycerides among 32 diabetic patients could be used as a predictor of myocardial infarction. On the other hand, Syvanne at al. and Mero et al. (33, 34) did not find an association between nonfasting triglycerides and cardiovascular disease among 30 and 43 patients with diabetes, respectively. Reyes-Soffer et al. (35) also found that after a fat-loading test, there was no association between nonfasting triglycerides and cardiovascular disease in 164 patients with diabetes. Although we have shown in the present study that the increase in triglycerides after normal food intake is modest in individuals with diabetes, and similar to that seen in individuals without diabetes, we were not able to test whether nonfasting lipids, lipoproteins, and apolipoproteins were associated with increased risk of cardiovascular disease in individuals with diabetes. This result occurred because we had only 2270 individuals with diabetes, and because, at this time, we have access only to limited follow-up and, thus, too few incident cardiovascular end points for meaningful statistical analyses. Nevertheless, future research clearly documenting that nonfasting lipid, lipoproteins, and apolipoproteins in patients with diabetes mellitus can be used for cardiovascular risk prediction similarly to how these measures are used in the nondiabetic population (4, 6) could further argue for a general change to make lipid profile measurements in the nonfasting state in individuals with diabetes rather than the fasting state.

One limitation of our study was that our measurements were not acquired from the same individuals at the different times since the last meal. Additionally, the small numbers of participants in the fasting state decreased the power to detect significant changes, particularly among individuals with diabetes. A potential limitation was the small number of individuals with diabetes in the study (nondiabetic patients, n = 56 164, and diabetic patients, n = 2270). Another limitation was the low participation rate; of the invited individuals, only 45% decided to participate in the study. Finally, because all participants were whites of Danish descent, our findings may not necessarily apply to other ethnic groups.

In conclusion, plasma triglycerides increased only a maximum of 0.2 mmol/L after normal food intake in both diabetic and nondiabetic individuals. Reduction in LDL cholesterol observed after normal food intake in both diabetic and nondiabetic individuals most

likely was caused by hemodilution due to fluid intake. Apolipoprotein B concentrations did not change after normal food intake, and non-HDL cholesterol also was found to be quite stable. These data may be useful for discussion during revisions of guidelines for lipid measurements in individuals with or without diabetes.

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