The difference between fasting and non-fasting lipid measurements is not related to statin treatment

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Background: Non-fasting blood samples are routinely used to assess plasma lipid profiles except in patients with severe hypertriglyceridemia according to the previous consensus. However, the impact of statin use on non-fasting plasma lipid measurements has not been thoroughly evaluated.

Methods: In this cross-sectional study, 686 patients with normal triglyceride (TG) levels, who were hospitalized due to chest pain, were enrolled. Fasting (8–12 h) and non-fasting (2–4 h after breakfast) lipid profiles were measured on the second day of admission. Patients were divided into the non-statin (n=499) group and statin treatment (n=187) group. Differences in fasting and non-fasting lipid profiles between the statin and non-statin groups were compared.

Results: The mean age of participants was 57±13 years, and 54.4% were male. A linear correlation was observed between fasting and non-fasting lipid profiles. Although a postprandial impact on lipid parameters was observed, the general pattern of differences between fasting and non-fasting lipids was similar in both groups. Additionally, the diff(%) [(non-fasting-fasting)/fasting ×100%] of lipid panels did not vary by statin treatment. Moreover, no effects of statin types or duration of use on non-fasting lipid profiles were identified.

Conclusions: The current study found fasting and non-fasting lipid panels were similar in individuals with or without statin treatment. Non-fasting lipid panels were not significantly affected by statin types or duration of use, suggesting that non-fasting lipid measurement is an acceptable test for patients receiving statin treatment.

Keywords: Non-fasting; statin; triglyceride (TG); cholesterol

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Introduction

People mainly live in the non-fasting state during a regular 24-hour cycle. Therefore, non-fasting lipid panels may be a reliable indicator of average lipid concentration level because the fasting state only occurs after fasting for at least 8 hours (1). The advantage of non-fasting over fasting lipid measurements is a simplified blood collection process for patients and physicians that is suitable for children, the elderly, and diabetic patients. For convenience, Denmark’s health services laboratories recommended implementation of a random non-fasting profile test in 2009 (2). Numerous clinical trials have shown that non-fasting low-density
lipoprotein cholesterol (LDL-C) has prognostic value that is similar to fasting levels. Non-fasting triglyceride (TG) levels are associated with an increased risk of coronary heart disease (CHD), similar to the increased risk associated with fasting concentrations (3). This observation has led to the notion that non-fasting lipids may be an equivalent or better predictor of cardiovascular conditions since non-fasting lipid profiles can reflect real status of circulating lipids (4).

Non-fasting lipid measurements are not “universally applicable”, and may require additional fasting lipid testing under certain clinical conditions. First, an additional laboratory test is required if non-fasting samples are initially analyzed for glucose or therapeutic drug monitoring. Second, the European consensus has recommended that laboratories offer re-measurement of fasting TGs if non-fasting TG levels are ≥350 mg/dL, because TG concentrations are more stable in the fasting state (1). Additionally, patients recovering from hypertriglyceridemia-induced pancreatitis or with diagnosed hypertriglyceridemia (TG ≥200 mg/dL according to American Heart Association guidelines) should be assessed fasting lipids during clinic follow-up (5). Finally, medications that can cause hypertriglyceridemia may affect non-fasting lipid profiles, thus emphasizing the need for repeated fasting measurements.

The impact of lipid-lowering medications on non-fasting lipid profiles has not been thoroughly evaluated. Statins, the most widely used lipid-lowering drugs, are known to reduce LDL-C by up to 50% and decrease TGs by 20% (6). Although non-fasting samples have been collected in several clinical trials following statin therapies (7-9), little information is currently available regarding differences between fasting and non-fasting lipid measurements in statin-treated individuals (10). In this study, we aimed to evaluate whether non-fasting lipid testing is clinically acceptable in patients receiving statin therapy and to examine the impact of statin types and duration of use on non-fasting lipid tests. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-20-3962).

Methods

Study population

The study cohort was prospectively designed to examine the difference between fasting and non-fasting lipid profiles. The study complied with the Declaration of Helsinki (as revised in 2013) and was approved by the hospital’s ethical review board (Fu Wai Hospital & National Center for Cardiovascular Diseases, Beijing, China, approval number: 2013-442). Informed written consents were obtained from all patients enrolled in this study.

From April 2015 to October 2018, 1,280 patients, scheduled for coronary angiography due to angina-like chest pain, were recruited at Fuwai Hospital (Figure 1). Patients with complete baseline demographic data and lipid tests (including fasting and non-fasting blood samples) were selected for this study. Sixty-one patients were excluded due to missing non-fasting blood samples, 458 patients were excluded because they had known hypertriglyceridemia (TG ≥200 mg/dL), and 47 patients were excluded due to missing values, severe hepatic or renal insufficiency, thyroid dysfunction, systemic inflammatory disease, or malignant tumor. Patients receiving other lipid-lowering therapies, or lower-intensity or high-intensity statin therapy before admission (n=28) were also excluded. Finally, 686 patients were enrolled in the final analysis and assigned to either moderate-intensity statin therapy before admission (n=187; statin group) or without statin therapy before admission (n=499; non-statin group).

Fasting blood samples were collected on the second day of admission following an 8–12-hour period of fasting; non-fasting blood samples were collected on the same day 2–4 hours after breakfast (1,11). High-intensity statin therapy was defined as equivalent to atorvastatin 40/80 mg/d or rosvastatin 20/40 mg/d. Moderate-intensity statin therapy was defined as equivalent to atorvastatin 10/20 mg/d, rosuvastatin 5/10 mg/d, simvastatin 20/40 mg/d, pravastatin 40/80 mg/d or pitavastatin 2/4 mg/d. Low-intensity statin therapy was defined as simvastatin 10 mg/d, pravastatin 10/20 mg/d or pitavastatin 1 mg/d (5). Hypertriglyceridemia was defined as a TG concentration ≥200 mg/dL, according to American or Chinese panels (12).

Fasting and non-fasting lipid profiles, including total cholesterol (TC), TG, LDL-C, high-density lipoprotein cholesterol (HDL-C), remnant cholesterol, and non-HDL-C, were analyzed in all participants. Remnant cholesterol was calculated as TC minus LDL-C minus HDL-C, which was the cholesterol content of all triglyceride-rich lipoproteins, including chylomicron remnants, very-low-density lipoprotein (VLDL), and intermediate-density lipoproteins (IDL) in the fasting or non-fasting states (13). Non-HDL-C was calculated as TC minus HDL-C, equivalent to the combined LDL-C, remnant cholesterol, and lipoprotein(a) cholesterol. Calculated LDL-C was defined by Friedewald equation as follows: LDL-C (mg/dL) = TC (mg/dL) –
HDL-C (mg/dL) – TG (mg/dL)/5. The diff(%)s of lipid panels were calculated as follows: (non-fasting – fasting)/fasting ×100%.

Hypertension was defined as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg, and/or currently taking antihypertensive drugs, and/or self-reported history of hypertension (14). Diabetes mellitus was defined by fasting plasma glucose ≥7.0 mmol/L, the 2-h plasma glucose of the oral glucose tolerance test ≥11.1 mmol/L, glycated hemoglobin ≥6.5%, and/or current use of hypoglycemic drugs or insulin, and/or self-reported history of diabetes (15). Body mass index (BMI) was calculated by height and weight (16).

**Laboratory examination**

Blood samples were collected through venipuncture and analyzed by clinical laboratory. Lipid profiles were measured using an automatic biochemistry analyzer (Hitachi 7150, Tokyo, Japan) by an enzymatic assay (17). In detail, TC was measured by the cholesterol oxidase-p-aminophenazone method (CHOD-PAP, Cholesterol kit, BioSino Biotechnology & Science Inc., Beijing, China). LDL-C was analyzed by the selective solubilization method (Low Density Lipid Cholesterol Test Kit, Kyowa Medex, Tokyo, Japan). HDL-C was determined by a similar method (Determiner L HDL, Kyowa Medex, Tokyo, Japan). Lp(a) was assayed by an immunoturbidimetry method according to the manufacturer’s guide as previously described [LASAY Lp(a) auto; SHIMA Laboratories, Tokyo, Japan] with a normal value of <30 mg/dL (18). HbA1c was measured using a Tosoh Automated Glycohemoglobin Analyzer (HLC-723G8, Tokyo, Japan).

**Statistical analysis**

Continuous variables are shown as mean ± standard deviation (SD) or median [interquartile range (IQR)]. Categorical variables are expressed as number (percentage). Differences between groups were analyzed using Student’s t-tests and χ² tests. Spearman rank correlation coefficients (r) were used to assess correlations between fasting and non-fasting lipid profiles. Fasting and non-fasting lipid profiles were compared using a nonparametric test of two paired samples (Wilcoxon signed-rank test). The diff(%)s in individuals with or without statins were compared by the Mann-Whitney μ test. The Bland-Altman analysis was conducted to assess agreement.
between fasting and non-fasting lipid tests. Statistical analyses were performed using SPSS software (version 25, SPSS, Chicago, Illinois, USA). All tests were two-sided and defined statistical significance by \( P<0.05 \).

**Results**

**Baseline characteristics**

The final dataset included 686 patients, with 187 assigned to the statin group and 499 assigned to the non-statin group. Baseline characteristics of participants in both groups are summarized in Table 1. The mean age of participants was 57±13 years, and 54.4% were male. There were no significant differences between the two groups in baseline variables, history of diabetes, or alcohol consumption. Notably, the percentage of participants with coronary artery disease (CAD) and hypertension was higher in the statin group. Patients with statin therapy were prescribed more aspirin and angiotensin-converting enzyme inhibitor (ACEI) in the hospital. In addition, the proportion of laboratory tests was similar in both groups.

**Changes and correlations between fasting and non-fasting lipids**

There were significant differences between fasting and non-fasting levels for all lipid parameters (\( P<0.001 \)). As shown in Table 2, a slight increase in the median (IQR) levels of TGs and remnant cholesterol was observed from the fasting to the non-fasting state. In contrast, a minor decrease in the median concentrations of TC, HDL-C, LDL-C and non-HDL-C was found from the fasting to the non-fasting state.

The absolute change in postprandial lipid levels was +0.19 mmol/L for TG, −0.05 mmol/L for TC, −0.02 mmol/L for HDL-C, −0.10 mmol/L for direct LDL-C, −0.13 mmol/L for calculated LDL-C, +0.06 mmol/L for remnant cholesterol and −0.03 mmol/L for non-HDL-C. The Bland-Altman analysis showed that the difference between fasting and non-fasting levels was within the total acceptable error allowed for each lipid parameter (Figure 2). Moreover, fasting lipid levels correlated well with non-fasting lipid levels, and further examination showed similar a linear correlation (Figure 3).

**Comparison between fasting and non-fasting lipids in statin and non-statin groups**

Mean differences between fasting and non-fasting lipid concentrations were similar in patients with and without statin treatment (Table 2). There were no significant differences for all lipid parameters between the statin and non-statin groups. In addition, non-HDL-C levels were not influenced by food intake in the statin-treated group, but median concentrations levels decreased by −0.05 (−0.30 to 0.21) mmol/L in the non-statin group.

Furthermore, the diff(\%)s [(non-fasting – fasting)/fasting ×100\%] for all lipid variables were not statistically different between the statin and non-statin groups. Diff(\%)s of TG were 16.5% in the statin-treated and 16.1% in the non-statin group. Similarly, the diff(\%)s were −0.6% and −1.1% for TC, −3.9% and −2.1% for HDL-C, −4.8% and −2.9% for direct LDL-C, −5.4% and −5.3% for calculated LDL-C, and 14.8% and 12.0% for remnant cholesterol in the statin and non-statin groups, respectively. Additionally, the diff(\%)s for non-HDL-C were modestly different between the statin (0.0%) and the non-statin groups (−1.5%).

**Comparison between fasting and non-fasting lipids in statin types, and duration of use**

Among all participants in the statin-treated group, 132 patients were prescribed moderate-intensity atorvastatin (ATO) or rosvastatin (ROS), while 55 patients were prescribed other types of statins. Median difference values and diff(\%)s for all lipid parameters were not significantly different between patients prescribed ATO or ROS and those prescribed other types of statins (Table 3). Similar results were found in individuals prescribed moderate-intensity statin therapy for 3 to 12 months and individuals with statin treatment for at least 1 year. The diff(\%)s for each lipid parameter were not statistically different when comparing short-term (<1 year) with long-term (>1 year) statin therapy (Table 4). Therefore, fasting and non-fasting lipids were not affected by statin types or duration of use.

**Discussion**

In this cross-sectional study, we found that the general pattern of differences between fasting and non-fasting lipid levels were similar in statin and non-statin groups. Diff(\%)s for all lipid parameters were not statistically significant in both groups regardless of statin types or duration of use. These findings suggest that non-fasting lipid measurements may be reliable for patients currently receiving statin therapy who do not have hypertriglyceridemia.

Previous studies, including the Copenhagen General
| Characteristics                  | Statin group (N=187) | Non-statin group (N=499) | P value |
|---------------------------------|----------------------|--------------------------|---------|
| **Baseline characteristics**    |                      |                          |         |
| Age, years                      | 56 (±12)             | 55 (±13)                 | 0.987   |
| Male, n (%)                     | 115 (61.5)           | 257 (51.6)               | 0.026   |
| BMI, kg/m²                       | 25.4 (±3.5)          | 24.6 (±3.7)              | 0.012   |
| HR, bpm                          | 71 (±11)             | 71 (±10)                 | 0.878   |
| SBP, mmHg                       | 127 (±17)            | 126 (±20)                | 0.558   |
| DBP, mmHg                       | 79 (±11)             | 78 (±12)                 | 0.547   |
| **History, n (%)**              |                      |                          |         |
| CAD                             | 186 (71.7)           | 249 (50.0)               | <0.001  |
| Hypertension                    | 104 (55.6)           | 231 (46.2)               | 0.044   |
| Diabetes mellitus               | 43 (23.0)            | 87 (17.5)                | 0.126   |
| Alcohol consumption             | 59 (31.6)            | 138 (27.7)               | 0.373   |
| **Laboratory test**             |                      |                          |         |
| WBC, 10⁹/L                      | 6.12 (±1.66)         | 5.88 (±1.56)             | 0.089   |
| Neutrophil, 10⁹/L               | 3.63 (±1.38)         | 3.44 (±1.22)             | 0.091   |
| Platelet, 10⁹/mm³               | 221 (±58)            | 222 (±58)                | 0.860   |
| FT3, pg/mL                      | 2.96 (±0.36)         | 2.93 (±0.59)             | 0.565   |
| FT4, ng/dL                      | 1.11 (±0.18)         | 1.13 (±0.22)             | 0.44    |
| Lp(a), mg/dL                    | 158 [66, 412]        | 138 [66, 281]            | 0.125   |
| **In-hospital medication, n (%)**|                      |                          |         |
| Aspirin                         | 145 (77.5)           | 308 (61.8)               | 0.001   |
| Clopidogrel                      | 96 (51.3)            | 215 (43.0)               | 0.176   |
| Calcium-channel blockers        | 45 (24.1)            | 103 (20.7)               | 0.639   |
| ACEI                            | 28 (15.0)            | 43 (8.6)                 | 0.031   |
| ARB                             | 32 (17.1)            | 95 (19.1)                | 0.350   |
| **Types of statin, n (%)**      |                      |                          |         |
| Simvastatin                     | 1 (0.5)              | 0 (0)                    | 0.607   |
| Atorvastatin                    | 36 (19.3)            | 20 (4.0)                 | <0.001  |
| Pravastatin                     | 1 (0.5)              | 2 (0.4)                  | 1.000   |
| Rosuvastatin                    | 38 (20.3)            | 29 (5.8)                 | <0.001  |
| Pitavastatin                    | 63 (33.7)            | 146 (29.3)               | 0.264   |

Data are mean (± SD), median [interquartile range] and number (%) of patients. BMI, body mass index; HR, heart rate; SBP, systolic blood pressure; DBP, diastolic blood pressure; CAD, coronary artery disease; WBC, white blood cell; FT3, free triiodothyronine; FT4, free thyroxine; Lp(a), lipoprotein(a); ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blockers.
| Measurement (mmol/L) | Total (N=686); median (Q1–Q3) | Statin group (N=187); median (Q1–Q3) | Non-statin group (N=499); median (Q1–Q3) | P value* for trend |
|---------------------|---------------------------------|--------------------------------------|------------------------------------------|--------------------|
| TG                  |                                 |                                      |                                          |                    |
| Fasting             | 1.22 (0.95 to 1.51)             | 1.25 (0.99 to 1.52)                 | 1.21 (0.93 to 1.50)                     |                    |
| Non-fasting         | 1.45 (1.12 to 1.78)             | 1.54 (1.16 to 1.82)                 | 1.44 (1.10 to 1.76)                     | 0.399              |
| Difference          | 0.19 (0.00 to 0.42)             | 0.20 (0.00 to 0.46)                 | 0.19 (0.00 to 0.41)                     |                    |
| Diff(%)             | 16.20%                          | 16.50%                               | 16.10%                                  | 0.723              |
| TC                  |                                 |                                      |                                          |                    |
| Fasting             | 4.52 (3.77 to 5.41)             | 4.16 (3.50 to 5.24)                 | 4.61 (3.89 to 5.44)                     |                    |
| Non-fasting         | 4.35 (3.68 to 5.17)             | 4.03 (3.40 to 5.01)                 | 4.47 (3.84 to 5.21)                     |                    |
| Difference          | –0.05 (–0.44 to 0.18)           | –0.02 (–0.43 to 0.17)               | –0.05 (–0.44 to 0.19)                   | 0.870              |
| Diff(%)             | –1.00%                          | –0.60%                               | –1.10%                                  | 0.871              |
| HDL-C               |                                 |                                      |                                          |                    |
| Fasting             | 1.17 (0.96 to 1.41)             | 1.10 (0.93 to 1.32)                 | 1.18 (0.98 to 1.47)                     |                    |
| Non-fasting         | 1.11 (0.91 to 1.34)             | 1.04 (0.84 to 1.25)                 | 1.15 (0.93 to 1.36)                     |                    |
| Difference          | –0.02 (–0.16 to 0.06)           | –0.04 (–0.18 to 0.04)               | –0.02 (–0.16 to 0.06)                   | 0.224              |
| Diff(%)             | –2.40%                          | –3.90%                               | –2.10%                                  | 0.118              |
| Direct LDL-C        |                                 |                                      |                                          |                    |
| Fasting             | 3.00 (2.38 to 3.69)             | 2.73 (2.05 to 3.65)                 | 3.08 (2.48 to 3.69)                     |                    |
| Non-fasting         | 2.81 (2.23 to 3.53)             | 2.56 (1.85 to 3.32)                 | 2.88 (2.39 to 3.55)                     |                    |
| Difference          | –0.10 (–0.36 to 0.10)           | –0.13 (–0.42 to 0.07)               | –0.09 (–0.36 to 0.11)                   | 0.201              |
| Diff(%)             | –3.50%                          | –4.80%                               | –2.90%                                  | 0.080              |
| Remnant cholesterol |                                 |                                      |                                          |                    |
| Fasting             | 0.34 (0.22 to 0.46)             | 0.33 (0.22 to 0.49)                 | 0.34 (0.21 to 0.45)                     |                    |
| Non-fasting         | 0.40 (0.25 to 0.56)             | 0.45 (0.24 to 0.62)                 | 0.40 (0.25 to 0.53)                     |                    |
| Difference          | 0.06 (–0.08 to 0.22)            | 0.08 (–0.05 to 0.26)                | 0.06 (–0.09 to 0.21)                    | 0.091              |
| Diff(%)             | 12.80%                          | 14.80%                               | 12.00%                                  | 0.531              |
| Non-HDL-C           |                                 |                                      |                                          |                    |
| Fasting             | 3.35 (2.67 to 4.05)             | 3.02 (2.33 to 4.03)                 | 3.44 (2.78 to 4.08)                     |                    |
| Non-fasting         | 3.20 (2.62 to 3.93)             | 2.96 (2.41 to 3.87)                 | 3.29 (2.75 to 3.93)                     |                    |
| Difference          | –0.03 (–0.29 to 0.17)           | 0.00 (–0.27 to 0.20)                | –0.05 (–0.30 to 0.21)                   | 0.596              |
| Diff(%)             | –1.00%                          | 0.00%                                | –1.50%                                  | 0.474              |
| Calculated LDL-C    |                                 |                                      |                                          |                    |
| Fasting             | 2.76 (2.08 to 3.43)             | 2.44 (1.76 to 3.41)                 | 2.87 (2.29 to 3.43)                     |                    |
| Non-fasting         | 2.56 (1.98 to 3.22)             | 2.28 (1.69 to 3.04)                 | 2.63 (2.11 to 3.23)                     |                    |
| Difference          | –0.13 (–0.40 to 0.06)           | –0.10 (–0.45 to 0.09)               | –0.12 (–0.39 to 0.05)                   | 0.904              |
| Diff(%)             | –5.30%                          | –5.40%                               | –5.30%                                  | 0.723              |

*, P<0.05 suggests significant difference. P value for difference between statin and non-statin group and Diff(%) is calculated by Mann-Whitney U test. TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
Population Study, the Women’s Health Study in the USA, the National Health and Nutrition Examination Survey in the USA, and Calgary Laboratory Services in Canada, have examined the utility of non-fasting lipid testing to define standard lipid parameters. Their results indicated that non-fasting lipid profiles changed minimally in response...
Average postprandial changes were +0.3 mmol/L for TG, −0.2 mmol/L for TC, −0.1 mmol/L for HDL-C, and −0.2 mmol/L for LDL-C. Although the extent of changes for these lipid parameters in our study differed slightly from the average values reported above, the trend we observed were identical to the findings of these large clinical trials. It is worth mentioning that non-HDL-C levels were similar in the fasting and non-fasting state during the study. Theoretically, non-HDL-C is equivalent to the combined LDL-C and remnant cholesterol. Although LDL-C decreased and remnant cholesterol increased in the non-fasting state, non-HDL-C levels remained unchanged. The reason behind this observation could be that non-HDL-C levels were calculated by TC and HDL-C levels, and both parameters decreased negligibly after breakfast in the statin group.

Fasting lipid panels have been the standard in clinical practice for the past half-century since the fasting TG levels were recommended in the 1967 classification of hyperlipidemia. Since then, fasting lipids have been widely used in real-world clinical practice to reduce measurement variability for TG and TC. Although fasting lipids may lead to a more accurate Friedewald-calculated LDL-C, the inconvenience of fasting lipid measurement has decreased patient compliance for lipid analysis. Recent

### Table 3 Comparison between fasting and non-fasting lipid profiles stratified by types of statin

| Measurement (mmol/L) | ATO or ROS (N=132) | Other types (N=55) | P value* for Diff(%) |
|----------------------|--------------------|--------------------|---------------------|
|                      | Median (Q1–Q3) | Difference (Q1–Q3); Diff(%) | Median (Q1–Q3) | Difference (Q1–Q3); Diff(%) |                      |
| **TG**               |                  |                    |                    |                      |
| Fasting              | 1.24 (0.98 to 1.53) | 0.17 (−0.02 to 0.42) | 1.32 (1.03 to 1.52) | 0.28 (0.00 to 0.53) | 0.186 |
| Non-fasting          | 1.48 (1.15 to 1.78) | 13.7%              | 1.64 (1.23 to 1.95) | 26.4%                |
| **TC**               |                  |                    |                    |                      |
| Fasting              | 4.07 (3.48 to 5.24) | −0.02 (−0.41 to 0.18) | 4.33 (3.59 to 5.37) | −0.05 (−0.44 to 0.11) | 0.816 |
| Non-fasting          | 4.05 (3.28 to 5.05) | −0.4%              | 3.96 (3.51 to 5.01) | −1.0%                |
| **HDL-C**            |                  |                    |                    |                      |
| Fasting              | 1.11 (0.94 to 1.30) | −0.03 (−0.18 to 0.04) | 1.08 (0.92 to 1.40) | −0.08 (−0.19 to 0.03) | 0.390 |
| Non-fasting          | 1.05 (0.85 to 1.25) | −2.9%              | 1.03 (0.82 to 1.25) | −7.1%                |
| **Direct LDL-C**     |                  |                    |                    |                      |
| Fasting              | 2.64 (2.04 to 3.69) | −0.13 (−0.44 to 0.10) | 2.92 (2.06 to 3.46) | −0.14 (−0.36 to 0.07) | 0.910 |
| Non-fasting          | 2.56 (1.81 to 3.37) | −4.8%              | 2.60 (2.01 to 3.21) | −4.9%                |
| **Remnant cholesterol** |            |                    |                    |                      |
| Fasting              | 0.32 (0.22 to 0.49) | 0.05 (−0.05 to 0.29) | 0.37 (0.22 to 0.50) | 0.09 (−0.03 to 0.25) | 0.245 |
| Non-fasting          | 0.43 (0.24 to 0.62) | 14.6%              | 0.47 (0.28 to 0.62) | 15.6%                |
| **Non-HDL-C**        |                  |                    |                    |                      |
| Fasting              | 3.01 (2.26 to 4.03) | 0.00 (−0.30 to 0.21) | 3.13 (2.48 to 4.03) | 0.00 (−0.25 to 0.16) | 0.906 |
| Non-fasting          | 2.96 (2.25 to 3.88) | 0.0%               | 2.99 (2.57 to 3.87) | 0.0%                 |
| **Calculated LDL-C** |                  |                    |                    |                      |
| Fasting              | 2.38 (1.76 to 3.52) | −0.07 (−0.48 to 0.11) | 2.81 (2.24 to 3.43) | −0.13 (−0.39 to 0.05) | 0.954 |
| Non-fasting          | 2.32 (1.55 to 3.08) | −5.0%              | 2.60 (2.06 to 3.22) | −5.5%                |

* P<0.05 suggests significant difference. P value for diff(%) is calculated by Mann-Whitney U test between different types of statin subgroups. ATO, atorvastatin; ROS, rosuvastatin; TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.
Table 4 Comparison between fasting and non-fasting lipid profiles stratified by durations of statin treatment

| Measurement (mmol/L) | Statin therapy <1 year (N=165) | Statin therapy ≥1 year (N=22) | P value* for Diff(%) |
|---------------------|---------------------------------|--------------------------------|---------------------|
|                     | Median (Q1–Q3)                  | Difference (Q1–Q3); Diff(%)   | Median (Q1–Q3)      | Difference (Q1–Q3); Diff(%) |                     |
| TG                  |                                 |                                |                     |                                 |                     |
| Fasting             | 1.21 (0.94 to 1.49)             | 0.21 (0.00 to 0.46)            | 1.53 (1.27 to 1.70) | 0.12 (−0.04 to 0.37)           | 0.205               |
| Non-fasting         | 1.46 (1.12 to 1.82)             | 17.4%                          | 1.70 (1.58 to 1.91) | 7.2%                            |                     |
| TC                  |                                 |                                |                     |                                 |                     |
| Fasting             | 4.13 (3.50 to 5.23)             | −0.04 (−0.40 to 0.17)          | 4.56 (3.20 to 5.90) | −0.01 (−0.98 to 0.27)          | 0.500               |
| Non-fasting         | 4.03 (3.48 to 5.03)             | −0.7%                          | 4.01 (3.19 to 4.77) | −0.3%                           |                     |
| HDL-C               |                                 |                                |                     |                                 |                     |
| Fasting             | 1.13 (0.95 to 1.34)             | −0.04 (−0.18 to 0.04)          | 0.92 (0.78 to 1.17) | −0.04 (−0.25 to 0.05)          | 0.496               |
| Non-fasting         | 1.07 (0.87 to 1.26)             | −3.2%                          | 0.78 (0.69 to 1.09) | −3.3%                           |                     |
| Direct LDL-C        |                                 |                                |                     |                                 |                     |
| Fasting             | 2.68 (2.05 to 3.59)             | −0.13 (−0.38 to 0.07)          | 3.13 (1.99 to 4.32) | −0.15 (−0.98 to 0.18)          | 0.427               |
| Non-fasting         | 2.58 (1.91 to 3.31)             | −4.7%                          | 2.39 (1.70 to 3.40) | −5.9%                           |                     |
| Remnant cholesterol |                                 |                                |                     |                                 |                     |
| Fasting             | 0.32 (0.22 to 0.49)             | 0.08 (−0.04 to 0.26)           | 0.43 (0.24 to 0.57) | 0.05 (−0.11 to 0.38)           | 0.642               |
| Non-fasting         | 0.45 (0.24 to 0.60)             | 14.8%                          | 0.48 (0.35 to 0.64) | 14.1%                           |                     |
| Non-HDL-C           |                                 |                                |                     |                                 |                     |
| Fasting             | 3.01 (2.33 to 3.93)             | 0.00 (−0.25 to 0.21)           | 3.49 (2.22 to 4.90) | 0.00 (−0.82 to 0.21)           | 0.320               |
| Non-fasting         | 2.96 (2.42 to 3.89)             | 0.0%                           | 2.93 (2.14 to 3.82) | 0.0%                            |                     |
| Calculated LDL-C    |                                 |                                |                     |                                 |                     |
| Fasting             | 2.38 (1.76 to 3.36)             | −0.10 (−0.41 to 0.10)          | 2.86 (1.56 to 4.10) | −0.11 (−0.84 to 0.06)          | 0.516               |
| Non-fasting         | 2.29 (1.70 to 3.04)             | −6.1%                          | 2.17 (1.37 to 3.16) | −3.3%                           |                     |

*, P<0.05 suggests significant difference. P value for diff(%) is calculated by Mann-Whitney U test between short-term and long-term statin subgroups. TG, triglyceride; TC, total cholesterol; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol.

studies have demonstrated the reliability of non-fasting TG for predicting risk of myocardial infarction, ischemic heart disease, and cardiovascular death, suggesting that non-fasting lipids may be useful for cardiovascular risk prediction (25). A meta-analysis examining 68 prospective studies reported that non-fasting blood samples did not attenuate the value for cardiovascular risk prediction (26). Therefore, based on the present evidence, non-fasting lipids may be similar, or superior, to fasting lipids for cardiovascular risk predictions. Whether non-fasting lipid tests are suitable for the patients currently receiving statin therapy has not been resolved prior to our study. The utility of non-fasting lipids has been examined in at least three statin-related clinical trials, including the Heart Protection Study, the lipid-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT-LLA), and the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) (7-9). Unfortunately, these studies did not focus on the impact of statin therapy on non-fasting lipids. Previous large randomized clinical trials allocated statins to participants in a fixed manner, including type and dose, making it impossible to observe the effects of different statins on non-fasting lipid levels. Given the limitations of previous clinical trials mentioned above, we saw the opportunity to study the potential impact of statin treatment, including statin types and administration
duration, on non-fasting lipid tests. The current study design may have several advantages compared to previous studies regarding the impacts of statin use on non-fasting lipid tests. First, the fasting and non-fasting blood samples were assayed on the same day. In addition, the effects of different statins and administration duration on the lipid profile of non-fasting lipids were examined. Moreover, patients in the statin group received moderate-intensity statin therapy for at least 3 months before hospitalization without other types of lipid-lowering drugs, such as ezetimibe or fibrate. Finally, the study excluded patients with hypertriglyceridemia in advance to strictly control the main confounding factor, TG, in the measurement of non-fasting LDL-C. Hence, the present study might provide additional, novel information regarding the clinical implication of non-fasting lipid tests in real world practice.

Nevertheless, there were several limitations of the present study. First, sample sizes were relatively small, which might have contributed to the borderline significance for some analyses (Table 2). Hence, additional investigations with larger sample sizes are needed in the future. Second, a single-center study may be another limitation, as ethnic differences and different lifestyles may lead to different results between Western and Chinese populations. Since our research enrolled only the Chinese participants, the results need to be confirmed in other racial groups.

Conclusions

The current study on Chinese participants showed a general pattern of differences between fasting and non-fasting lipid profiles in the statin and non-statin groups. At the same time, the data also indicated that the differences between fasting and non-fasting lipid measurements were not affected by statin types or duration of use. These findings are novel and suggest that non-fasting lipid tests are clinically acceptable for patients receiving statin treatment.

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Footnote

Reporting Checklist: The authors present the study in accordance with the STROBE reporting checklist. Available at http://dx.doi.org/10.21037/atm-20-3962

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at: http://dx.doi.org/10.21037/atm-20-3962). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study complied with the Declaration of Helsinki (as revised in 2013) and was approved by the hospital’s ethical review board (Fu Wai Hospital & National Center for Cardiovascular Diseases, Beijing, China, approval number: 2013-442). Informed written consents were obtained from all patients enrolled in this study.

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