Associations between Blood Lipid Profiles and Risk of Myocardial Infarction Among Japanese Male Workers: 3M Study

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Aim: To examine whether fasting blood lipid profiles are associated with the risk of myocardial infarction among Japanese men.

Methods: We conducted a nested case-control study in the Morbidity of Myocardial Infarction Multicenter Study in Japan (3M Study). For each case of myocardial infarction entered in the 3M Study between 1997 and 2000, we randomly selected two controls, matched for age (±3 years), from among the participants in risk factor surveys with no history of myocardial infarction. A total of 723 male employees (241 cases and 482 controls) aged 35 to 65 years were enrolled in the present study.

Results: The subjects had significantly higher mean fasting LDL-cholesterol and triglyceride, and lower mean HDL-cholesterol than controls. The multivariable conditional odds ratio (95% confidence interval) for myocardial infarction after adjustment for known cardiovascular risk factors was 3.87 (1.27–11.7, p for trend <0.001) for total cholesterol [≥6.71 vs <4.65 mmol/L], 3.28 (1.12–9.60, p for trend=0.001) for LDL-cholesterol [≥4.64 vs <2.59 mmol/L], 0.17 (0.07–0.43, p for trend=0.001) for HDL-cholesterol [≥1.55 vs <1.03 mmol/L] and 3.03 (1.37–6.70, p for trend=0.01) for triglycerides [≥2.26 vs <1.13 mmol/L].

Conclusion: High total and LDL-cholesterol, low HDL-cholesterol and high triglycerides levels were independently associated with an increased risk of myocardial infarction among middle-aged Japanese male workers.

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Key words; LDL-cholesterol, HDL-cholesterol, Triglycerides, Myocardial infarction, Japanese

Introduction

Although mortality from ischemic heart disease is lower in Japan than in Western countries1, ischemic heart disease, half of which is accounted for by myocardial infarction, is one of the most common causes of death in Japan2–4. High total and LDL-cholesterol and low HDL-cholesterol are well-established risk factors in western countries5,6, but little evidence for LDL-cholesterol7 and HDL-cholesterol8 is available for Japanese, whose serum total cholesterol levels have increased consistently over the past 20 years9–14. Evidence for triglycerides is also limited15. Few studies have examined systematically the associations between blood lipid profiles and the risk of myocardial infarction in Japanese populations.

A total of 296 myocardial infarction patients were registered between 1997 and 2000 in the Morbidity of Myocardial Infarction Multicenter Study in Japan (3M Study) initiated by the authors (K.H. et al16). To examine whether blood lipid profiles are associated with the risk of myocardial infarction in middle-aged Japanese men, we conducted a nested...
Subjects and Methods

Study Population

The Morbidity of Myocardial Infarction Multicenter Study in Japan (3M Study) was initiated in 1997 with the participation of 76 companies with a medical center employing occupational physicians registered in all seven districts of urban areas of Japan. The details of the study methods were described in our previous paper\(^\text{10}\). The subjects were 390,539 employees aged 35 to 65 years, consisting of 133,099 employees (109,550 men, 23,549 women) from 41 workplaces (April 1994 to March 1997) and 257,440 (207,310 men, 50,130 women) from 76 workplaces (April 1997 to March 2000). There was one workplace in Hokkaido, 3 in Tohoku, 31 in Kanto, 7 in Chubu, 25 in Kinki, 5 in Chugoku-Shikoku, and 4 in Kyushu-Okinawa. These workplaces were located in cities of various population sizes; 40 workplaces were in 12 cities with more than 500,000; 27 workplaces in 22 cities with fewer than 500,000; and 9 workplaces were in rural areas. The surveyed workplaces covered the electrical, automobile, chemical, and machinery industries, as well as finance, insurance, information, communications, trading, and service companies.

Data for cardiovascular risk factors were obtained from the records of annual health examinations conducted by the companies and used as the baseline. From April 1997 to March 2000, we documented the incidence of myocardial infarction according to the criteria of the World Health Organization Multinational MONItoring of trends and determinants in the CArdiovascular disease Project (WHO MONICA project) while the subjects were employed\(^\text{17}\). They were not followed after their retirement.

Age-Matched Case-Control Study

We used an age-matched nested case-control design for the data analyses because the incidence or prevalence of myocardial infarction is very low among Japanese populations\(^\text{4, 18}\).

A total of 296 fatal and nonfatal myocardial infarction cases were registered from April 1997 to March 2000. There were only 3 cases of myocardial infarction among women, and thus the present subjects were restricted to men. Further, we excluded 52 patients (7 re-occurrences, 44 without data for complete lipid profiles and one with a triglyceride level over 8.8 mmol/L (802 mg/dL)) thus leaving 241 subjects (45 fatal, 221 defined and 5 possible acute myocardial infarctions) for the analyses.

For each case of myocardial infarction, we randomly selected two age-matched (± 3 years) controls from among the participants with no history of myocardial infarction until March 2000. Thus, 723 male employees (241 cases and 482 control subjects) were analyzed in the study.

Cardiovascular Risk Factors at Baseline Survey

We used the data of health examinations conducted within one year before the incidence of myocardial infarction for cases that occurred between 1994 and 2000. The controls were selected randomly from participants in 1999 and 2000 surveys in two workplaces. The data included body height and weight, systolic and diastolic blood pressure, serum total cholesterol, HDL-cholesterol, triglycerides and glucose, medication use for hypertension, hyperlipidemia and diabetes mellitus, smoking status (non-smoker, ex-smoker, < 20/day, 21–40/day and ≥ 41/day) and alcohol consumption (non-drinker, ex-drinker, < 1 cups/day, 1–2 cups/day and ≥ 3 cups/day). Blood samples in a fasting state were collected from all participants. We determined the body mass index (BMI) as weight (kg) divided by the square of height in meters (m\(^2\)). LDL-cholesterol was measured with the Friedewald formula as LDL-cholesterol = total cholesterol – HDL-cholesterol – 0.2*triglycerides\(^\text{19}\). A previous study showed no bias related to LDL-cholesterol levels among persons with < 8.8 mmol/L (< 802 mg/dL) of triglycerides\(^\text{20}\).

Hypertension was defined as systolic blood pressure ≥ 140 mmHg and/or diastolic blood pressure ≥ 90 mmHg and/or under treatment for hypertension. Glucose abnormality was defined as fasting blood glucose ≥ 6.11 mmol/L (110 mg/dL) and/or under treatment for diabetes mellitus. External quality control had been conducted for lipid measurement and other cardiovascular risk factors for each medical center according to the National Federation of Industrial Health Organization.

Diagnostic Criteria

The definitions of coronary events followed the criteria used in the WHO MONICA project\(^\text{17}\). Cases of silent MI and recurrence (a new event occurring more than 28 days after the previous MI) were also registered; however, we excluded recurrent MI for risk factor estimation of first-event MI from the present analyses. The details of event registration and diagnosis were described elsewhere\(^\text{10}\). Briefly, occupational physicians affiliated to the surveyed companies had received reports of absence and returns to work from business owners, and/or if the death certificate sug-
suggested MI, then the occupational physicians asked for a hospital record of care from the attending physician. Final diagnoses were made by a panel of three cardiologists licensed by the Japan Circulation Society. The details of event registration are shown elsewhere. Almost all participants undertook annual health examinations with electrocardiograms. Thus, silent MI within one year can be detected by changes in resting electrocardiogram (i.e., Q wave appearance).

The definition of sudden death was death from an unknown cause within 24 h after the onset of acute symptoms. Death within 28 days after the onset of MI was defined as fatal MI. All registered cases were reviewed independently by 3 reviewers who were members of the Japanese Circulation Society, and were classified as fatal (F1: definite myocardial infarction, F2: possible coronary death, F4: not myocardial infarction or coronary death, F9: unclassifiable) or nonfatal (NF1: definite myocardial infarction, NF2: possible myocardial infarction, NF4: not myocardial infarction). In the majority of patients, coronary arteriography and left ventriculography were performed during hospitalization, which we took into account in the diagnoses. When the assigned category differed among reviewers, the patient was re-assessed by the review board for final judgment. To allow comparison of our data with the MONICA project and with other Japanese domestic studies, the total number of MI and coronary deaths was calculated as F1 + F2 + F9 + NF1 + NF2.

Statistical Analysis

We used Student’s t test and the chi square test to compare the characteristics of cases and controls. The subjects were divided into four or five categories based on total cholesterol (<4.65, 4.65–5.15, 5.16–5.66, 5.67–6.70 and ≥6.70 mmol/L; <180, 180–199, 200–219, 220–259 and ≥260 mg/dL), LDL-cholesterol (<2.59, 2.59–3.08, 3.09–3.59, 3.60–4.63 and ≥4.64 mmol/L; <100, 100–119, 120–139, 140–179 and ≥180 mg/dL), HDL-cholesterol (<1.03, 1.03–1.28, 1.29–1.54 and ≥1.55 mmol/L; <40, 40–49, 50–59 and ≥60 mg/dL) and triglyceride (<1.13, 1.13–1.68, 1.69–2.25 and ≥2.26 mmol/L; <100, 100–149, 150–199 and ≥200 mg/dL). The odds ratio and 95% confidence interval (95% CI) were calculated using the conditional logistic regression model for age-matched odds ratio and multivariable odds ratio. Multivariable adjustment used serum lipid profiles (LDL-cholesterol, HDL-cholesterol and triglyceride) and cardiovascular risk factors.

The cardiovascular risk factors included a history of hypertension and glucose abnormality, treatment of hyperlipidemia (yes or no), BMI (metric variable), smoking status (non-smoker, ex-smoker, current smoker of <21/day, 21–40/day and ≥41/day) and alcohol consumption category (non-drinker, ex-drinker, current drinkers of <1 cups/day, 1–2 cups/day and ≥3 cups/day). We also calculated the odds ratio for 1 standard deviation increment of blood lipids. Triglycerides were log transformed since their distributions were not normal. Additionally, we calculated the odds ratio and 95% CI, stratified by the smoking status, a strong risk factor for coronary heart disease. After adjusting for cardiovascular risk factors, a test for the effect modification by smoking status was conducted with an interaction term generated by multiplying continuous variables of total, LDL- and HDL-cholesterol and triglycerides by smoking status. Statistical significance was defined as p < 0.05 for two-tailed analysis. All statistical analyses were performed with SAS 9.1 for Windows (SAS Institute Inc., Cary, NC).

Results

Table 1 shows the baseline characteristics of the cases and controls. Mean age ± standard deviation was 50.7 ± 5.4 for cases and 50.6 ± 5.6 for controls. Cases had higher mean height, BMI, systolic and diastolic blood pressure, serum LDL-cholesterol, triglyceride, glucose and lower mean HDL-cholesterol than controls. Moreover, they were more likely to have hypertension and diabetes mellitus and they were also likely to be current smokers.

Table 2 shows the conditional odds ratios of myocardial infarction according to lipid profiles. Compared with men with the lowest categories of lipid profiles, men with the highest categories of total and LDL-cholesterol and triglycerides had significantly higher age-matched odds ratios for myocardial infarction and those with the highest category of HDL-cholesterols had significantly lower odds ratios. After adjusting for other lipids and cardiovascular risk factors, these associations were weakened, but remained statistically significant. The multivariable odds ratios (95% confidence intervals) were 3.87 (95%CI: 1.27–11.7, p for trend < 0.001) for total cholesterol, 3.28 (95%CI: 1.12–9.60, p for trend = 0.001) for LDL-cholesterol, 0.17 (95%CI: 0.07–0.43, p for trend = 0.001) for HDL-cholesterol and 3.03 (95%CI: 1.37–6.70, p for trend = 0.01) for triglycerides.

Table 3 shows conditional odds ratios of myocardial infarction according to lipid profiles, stratified by smoking status. The multivariable conditional odds ratio (95% CI) of myocardial infarction among non-smokers was 1.43 (95%CI: 0.11–17.9, p for trend = 0.18) for total cholesterol, 1.09 (95%CI: 0.12–10.2, p
Table 1. Characteristics of subjects in case and control subjects

|                        | Case (n=241) | Control (n=482) | p-value  |
|------------------------|-------------|-----------------|----------|
| Age (year)             | 50.7 ± 5.4  | 50.6 ± 5.6      | 0.74     |
| Height (cm)            | 166.0 ± 5.8 | 169.2 ± 5.5     | <0.001   |
| Weight (kg)            | 65.9 ± 9.1  | 66.7 ± 8.6      | 0.25     |
| Body mass index (kg/m²)| 23.9 ± 2.8  | 23.3 ± 2.7      | 0.01     |
| Systolic blood pressure (mmHg) | 134.6 ± 16.4 | 122.9 ± 17.5 | <0.001   |
| Diastolic blood pressure (mmHg) | 82.7 ± 11.3 | 77.1 ± 11.3     | <0.001   |
| Fasting glucose (mmol/L)| 5.76 ± 0.93 | 5.25 ± 0.85     | <0.001   |
| Total cholesterol (mmol/L) | 3.63 ± 0.93 | 3.17 ± 0.80     | <0.001   |
| LDL-cholesterol (mmol/L) | 1.20 ± 0.32 | 1.49 ± 0.35     | <0.001   |
| Triglycerides (mmol/L)  | 2.04 ± 1.38 | 3.10 ± 0.79     | <0.001   |
| Current smokers (%)     | 71.1        | 41.3            | <0.001   |
| Current drinkers (%)    | 70.7        | 73.4            | 0.44     |
| Treatment of hyperlipidemia (%) | 7.6       | 7.3             | 0.88     |
| Glucose abnormality (%) | 28.2        | 15.8            | <0.001   |
| Hypertension (%)        | 30.7        | 46.5            | <0.001   |

Mean ± standard deviation
Current smokers: ≥1 cigarettes smoked per day.
Current drinkers: ≥1 cups per day.
Glucose abnormality: fasting blood glucose ≥6.11 mmol/L (110 mg/dL) and/or on treatment of diabetes mellitus.
Hypertension: Systolic blood pressure ≥140 mmHg and/or diastolic blood pressure ≥90 mmHg and/or on antihypertensive treatment.

Discussion

High total and LDL-cholesterol levels and low HDL-cholesterol levels were independently and linearly associated with an increased risk of myocardial infarction. The excess risk of myocardial infarction was observed in high triglycerides levels (≥2.26 mmol/L; 200 mg/dL) after adjustment for HDL-cholesterol levels and other cardiovascular risk factors.

The magnitudes of the positive association in the present study were similar to those reported from previous cohort studies in Americans or Europeans and a cohort study of Japanese. The magnitude of the inverse association with HDL-cholesterol was larger in Japanese than in Americans or Europeans, as reported in a previous Japanese study. Previous studies of Japanese and Americans, but not all, showed a linear association between serum triglyceride levels and the risk of myocardial infarction. In the Japanese study, non-fasting triglycerides were associated with the risk among men and women aged 40–69 years, residing in communities; a threefold excess risk was observed from the triglyceride level ≥1.89 mmol/L (167 mg/dL) compared with < 0.95 mmol/L (84 mg/dL).

Recently, the Women’s Health Study showed that non-fasting triglyceride levels are more predictive of the risk of cardiovascular events than fasting triglycerides; therefore, the weaker and non-linear association between triglycerides and the risk in the present study could be in part due to the use of fasting samples.

Although the magnitude and shape of associations with LDL-cholesterol and triglycerides vary among studies, the present study extended the evidence that LDL-cholesterol, HDL-cholesterol and triglycerides were significant predictors of myocardial infarction in Japanese middle-aged men. Associations of total and LDL-cholesterol and triglycerides with myocardial infarction did not vary, but HDL-cholesterol...
Table 2. Conditional odds ratio (OR) and 95% confidence interval (CI) of myocardial infarction according to lipid profiles

| Lipid categories | (Lower) | (Higher) | \( p \) for trend | OR per 1 SD Increment |
|------------------|---------|----------|------------------|-----------------------|
| Total cholesterol |         |          |                  |                       |
| Range, mmol/L    | <4.65   | 4.65–5.15| 5.16–5.66 | 5.67–6.70 | 6.71 + |
| Range, mg/dL     | <180    | 180–199 | 200–219 | 220–259 | 260 + |
| No. of cases      | 24      | 42       | 47     | 97      | 31     |
| No. of controls   | 122     | 99       | 126    | 113     | 22     |
| Age-matched OR    | 1.00    | 2.28 (1.29–4.04) | 1.88 (1.09–3.25) | 4.66 (2.73–7.97) | 8.03 (3.84–16.8) | <0.001 | 1.85 (1.54–2.22) |
| Multivariable OR  | 1.00    | 2.18 (0.97–4.90) | 1.81 (0.80–4.10) | 5.37 (2.32–12.4) | 3.87 (1.28–11.7) | <0.001 | 1.71 (1.29–2.27) |
| LDL-cholesterol   |         |          |                  |                       |
| Range, mmol/L    | <2.59   | 2.59–3.08| 3.09–3.59 | 3.60–4.63 | 4.64 + |
| Range, mg/dL     | <100    | 100–119 | 120–139 | 140–179 | 180 + |
| No. of cases      | 33      | 34       | 55     | 91      | 28     |
| No. of controls   | 104     | 126      | 121    | 112     | 19     |
| Age-matched OR    | 1.00    | 0.88 (0.51–1.52) | 1.43 (0.86–2.40) | 2.66 (1.61–4.38) | 5.43 (2.55–11.6) | <0.001 | 1.81 (1.51–2.17) |
| Multivariable OR  | 1.00    | 0.88 (0.41–1.89) | 1.93 (0.87–4.31) | 2.51 (1.18–5.35) | 3.28 (1.12–9.60) | 0.001 | 1.60 (1.23–2.08) |
| HDL-cholesterol   |         |          |                  |                       |
| Range, mmol/L    | <1.03   | 1.03–1.28| 1.29–1.54 | 1.55 + |
| Range, mg/dL     | <40     | 40–49   | 50–59 | 60 + |
| No. of cases      | 82      | 74       | 55     | 30     |
| No. of controls   | 33      | 112      | 145    | 192    |
| Age-matched OR    | 1.00    | 0.29 (0.18–0.49) | 0.16 (0.09–0.27) | 0.07 (0.04–0.12) | <0.001 | 0.36 (0.29–0.45) |
| Multivariable OR  | 1.00    | 0.46 (0.23–0.94) | 0.16 (0.07–0.38) | 0.17 (0.07–0.43) | 0.001 | 0.53 (0.38–0.75) |
| Triglycerides     |         |          |                  |                       |
| Range, mmol/L    | <1.13   | 1.13–1.68| 1.69–2.25 | 2.26 + |
| Range, mg/dL     | <100    | 100–149 | 150–200 | 200 + |
| No. of cases      | 57      | 77       | 33     | 74     |
| No. of controls   | 247     | 128      | 58     | 49     |
| Age-matched OR    | 1.00    | 2.57 (1.70–3.88) | 2.52 (1.47–4.33) | 7.29 (4.36–12.2) | <0.001 | 2.29 (1.87–2.79) |
| Multivariable OR  | 1.00    | 1.25 (0.67–2.31) | 0.94 (0.41–2.17) | 3.03 (1.37–6.70) | 0.01 | 1.65 (1.22–2.24) |

Multivariable OR: adjusted for high blood pressure, hyperglycemia, treatment of hyperlipidemia, body mass index, smoking status, alcohol consumption and other lipid profiles (HDL-cholesterol and triglycerides for total cholesterol mode) 
1SD: 0.91 mmol/L (35.0 mg/dL) for total cholesterol, 0.87 mmol/L (33.8 mg/dL) for LDL-cholesterol, 0.37 mmol/L (14.3 mg/dL) for HDL-cholesterol and 1.08 mmol/L (95.9 mg/dL) for triglycerides.

While mortality from coronary heart disease has declined in Japan since the 1960s, this decline was smaller for men aged 30–49 years residing in the Tokyo and Osaka metropolitan areas, where 17% of the total Japanese population resides, than for their counterparts in the rest of Japan. On the other hand, the incidence of coronary heart disease increased three-fold among urban male employees aged 40–59 years between the 1960s and the 1990s, and doubled among urban male residents aged 40–69 years between the 1980s and 2000s. Watanabe et al. reviewed that westernization of the lifestyle promotes the development of pre-clinical atherosclerosis in Japanese. According to the National Health and Nutrition Survey in Japan, dietary fat intake, especially animal fat, has increased, and serum total cholesterol levels have increased for both men and women, but blood pressure levels for both sexes and the prevalence of smoking for men declined from the 1960s to 1990s. These trends in coronary risk factors suggest that the contribution of dyslipidemia to the development of coronary heart disease has become more significant in Japanese populations, particularly middle-aged men.
Table 3. Conditional odds ratio (OR) and 95% confidence interval (CI) of myocardial infarction according to lipid profiles stratified by smoking status

| Lipid categories       | (Lower) | (Higher) | \( \rho \) for trend | \( \rho \) for interaction* | OR per 1 SD Increment |
|------------------------|---------|----------|-----------------------|-----------------------------|----------------------|
| Total cholesterol      |         |          |                       |                             |                      |
| Non-smokers            |         |          |                       |                             |                      |
| No. of cases           | 6       | 16       | 9                     |                             | 2.37 (1.45–3.87)     |
| Age-matched OR         | 1.00    | 1.08     | 9                     |                             | 1.07 (0.58–1.99)     |
| Multivariable OR       | 1.00    | 1.06     | 9                     |                             | 1.06 (0.58–1.99)     |
| Current smokers        |         |          |                       |                             |                      |
| No. of cases           | 18      | 31       | 22                    |                             | 2.08 (1.08–4.01)     |
| Age-matched OR         | 1.00    | 1.24     | 22                    |                             | 1.89 (1.38–2.59)     |
| Multivariable OR       | 1.00    | 1.20     | 22                    |                             | 1.52 (0.79–2.89)     |
| LDL-cholesterol        |         |          |                       |                             |                      |
| Non-smokers            |         |          |                       |                             |                      |
| No. of cases           | 11      | 18       | 8                     |                             | 1.89 (1.25–2.86)     |
| Age-matched OR         | 1.00    | 1.06     | 8                     |                             | 1.50 (0.79–2.89)     |
| Multivariable OR       | 1.00    | 1.05     | 8                     |                             | 1.47 (0.79–2.89)     |
| Current smokers        |         |          |                       |                             |                      |
| No. of cases           | 22      | 37       | 20                    |                             | 1.60 (1.22–2.11)     |
| Age-matched OR         | 1.00    | 1.05     | 20                    |                             | 1.81 (1.04–3.15)     |
| Multivariable OR       | 1.00    | 1.04     | 20                    |                             | 1.80 (1.03–3.15)     |
| HDL-cholesterol        |         |          |                       |                             |                      |
| Non-smokers            |         |          |                       |                             |                      |
| No. of cases           | 18      | 18       | 16                    |                             | 0.46 (0.30–0.72)     |
| Age-matched OR         | 1.00    | 0.99     | 16                    |                             | 0.94 (0.50–1.78)     |
| Multivariable OR       | 1.00    | 0.98     | 16                    |                             | 1.07 (0.50–1.78)     |
| Current smokers        |         |          |                       |                             |                      |
| No. of cases           | 64      | 37       | 14                    |                             | 0.40 (0.28–0.59)     |
| Age-matched OR         | 1.00    | 0.99     | 14                    |                             | 0.97 (0.50–1.78)     |
| Multivariable OR       | 1.00    | 0.98     | 14                    |                             | 1.06 (0.50–1.78)     |
| Triglycerides          |         |          |                       |                             |                      |
| Non-smokers            |         |          |                       |                             |                      |
| No. of cases           | 24      | 19       | 24                    |                             | 2.50 (1.59–3.95)     |
| Age-matched OR         | 1.00    | 1.02     | 24                    |                             | 2.70 (1.79–3.87)     |
| Multivariable OR       | 1.00    | 1.01     | 24                    |                             | 2.80 (1.80–3.90)     |
| Current smokers        |         |          |                       |                             |                      |
| No. of cases           | 33      | 58       | 50                    |                             | 2.07 (0.92–4.64)     |
| Age-matched OR         | 1.00    | 1.05     | 50                    |                             | 1.87 (1.06–3.30)     |
| Multivariable OR       | 1.00    | 1.04     | 50                    |                             | 1.86 (1.05–3.30)     |

Multivariable OR: adjusted for high blood pressure, hyperglycemia, treatment of hyperlipidemia, body mass index, alcohol consumption and other lipid profiles other lipid profiles (HDL-cholesterol and triglyceride for total cholesterol model, LDL-cholesterol

*\( \rho \)-values for interaction were estimated using a multivariable-adjusted model.

1SD: 0.91 mmol/L (35.0 mg/dL) for total cholesterol, 0.87 mmol/L (33.8 mg/dL) for LDL-cholesterol, 0.37 mmol/L (14.3 mg/dL) for HDL-cholesterol and 1.08 mmol/L (95.9 mg/dL; 0.58 (log trasformed)) for triglycerides.
with standardized surveillance for myocardial infarction. Thus, our findings could be more generalized for middle-aged Japanese men in companies than in rural communities, in selected urban companies or urban residents. The number of myocardial infarctions in the present study was much larger than in previous Japanese studies, and we conducted stratified analysis by smoking status.

There are several limitations of the present study. First, the subjects were only middle-aged male workers. Thus, the findings can not be generalized for women and elderly. Second, the follow-up period between lipid measurement and the onset of coronary heart disease in the present study was short, although a previous observational study indicated that associations between blood lipids and the risk of coronary heart disease might not be affected by the follow-up period. That study showed that hazard risks (95% CI) of coronary heart disease for 1 mmol/L increment of serum total cholesterol were 1.44 (1.23–1.68) for 0- to 5-year follow-up and 1.52 (1.31–1.76) for 5- to 10-year followed-up among middle-aged European men.

In conclusion, high total and LDL-cholesterol, low HDL-cholesterol and high triglyceride levels were found to be independently associated with an increased risk of myocardial infarction among middle-aged Japanese male workers.

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Appendix

The following persons participated in the 3M Study:

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