Distribution and Cardiovascular Risk Correlates of Serum Triglycerides in Young Japanese Adults

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Abstract: To examine the distribution and cardiovascular risk correlates of serum triglycerides, a cross-sectional population study based on annual health examinations at the workplace was performed in 2199 young Japanese adults aged 23 to 37 years. Triglyceride levels showed significant sex (male > female) differences, and the percentages of those with high triglycerides (≥ 150 mg/dl) were 9.4% for males and 0.8% for females. In terms of conjoint trait of dyslipidemia, 86.1% of males displayed normal levels of both triglycerides (< 150 mg/dl) and high-density lipoprotein (HDL) cholesterol (≥ 40 mg/dl), while 98.7% of females had normal values. Age- and sex-specific triglyceride levels above the 75th percentile (equivalent to 82–116 mg/dl for males and 56–63 mg/dl for females) increased the risk (odds ratio (OR)) for having obesity, hypertension, and hyperuricemia by 2.9 (95% confidence interval (CI)=2.0–4.3), 1.7 (CI=1.1–2.9), and 3.0 (CI=1.6–5.9), respectively. The respective ORs for triglyceride levels above the 75th percentile and HDL cholesterol below the 25th percentile (equivalent to 45–49 mg/dl for males and 58–63 mg/dl for females), compared with triglyceride levels the 75th percentile or less and HDL cholesterol levels the 25th percentile or more, were 8.7 (CI=5.8–12.9), 2.2 (CI=1.5–3.3), and 6.0 (CI=3.2–11.5). Our results suggest a threshold effect of triglyceride levels considered as normal on enhanced cardiovascular risk in young Japanese adults, especially in those with low HDL cholesterol levels.

Key words: Triglycerides, High-density lipoprotein cholesterol, Cardiovascular risk, Young adults, Japanese

Introduction

Although the role of triglycerides as an independent risk factor for coronary heart disease (CHD) remains elusive1, accumulated biologic evidence relating to triglycerides, atherosclerosis, and thrombosis has indicated the potential importance of triglycerides in the etiology of CHD1. A recent meta-analysis of 17 prospective studies in Europe and the United States showed that adjustment for high-density lipoprotein (HDL) cholesterol attenuated the relation between triglycerides and the risk for CHD, but the pooled relative risk estimates were statistically significant for both males and females2. More recently, a prospective study in Japan has demonstrated that serum triglyceride levels are independently related to the development of CHD among Japanese males and females who possess low mean values of serum triglycerides3. The National Cholesterol Education Program (NCEP) guidelines included considerations of triglyceride lowering in certain high-risk situations associated with fasting serum triglyceride levels higher than 200 mg/dl4. However, this cutpoint for serum triglycerides is considered to be high in terms of CHD risk assessment5-8, especially for young adults.

Although several population-based studies investigated serum lipids and lipoproteins in young adults9-13, few studies have focused specifically on serum triglycerides in terms
of cardiovascular risk in this age group\textsuperscript{9}. To our knowledge, there have been no other reports on the potential of serum triglycerides as a risk factor in an young Japanese adult population. In this report on a cross-sectional population study based on annual health examinations at the workplace, we examined the distribution and correlates of serum triglycerides in young Japanese adults aged 23 to 37 years.

Materials and Methods

Study population

A survey was conducted in May 1996 of employees of A Corporation, which is one of the biggest building contractors in Japan. The participants in the 1996 survey consisted of 2210 Japanese male office workers aged 23 to 37 years, and the participation rate was 99.5\%. The Industrial Safety and Health Law in Japan requires the employer to conduct annual health examinations of all employees; the employee data, which are anonymized, are available for research with the approval of the employer. We considered the return of self-administered questionnaires signed by the subjects to imply their consent to participate in the study. For the present study, only subjects without medications for dyslipidemia or hypertension (n=2199) were included in the analysis. The study population consisted of 75.5\% Japanese males and 24.5\% Japanese females.

Study items

The health examinations included medical history, physical examinations, anthropometric measurements, blood pressure measurements, biochemical measurements, and a question on alcohol intake and cigarette smoking. The participants were asked to fast for at least 8 hours and to avoid smoking and heavy physical activity for more than 2 hours before the examinations. Medical history and the history of use of prescribed drugs were assessed for each subject by the examining physicians. Body mass index (BMI) was used as a measure of overall obesity and was calculated as body weight/height\textsuperscript{2} (kg/m\textsuperscript{2}). After a 5-minute rest in a quiet room, systolic and diastolic blood pressures were measured on the right arm by using a standard mercury sphygmomanometer. After the measurement of blood pressures, blood samples were drawn from an antecubital vein. The serum and plasma were sent to a commercial laboratory for determination of total cholesterol, HDL cholesterol, triglycerides, and uric acid and fasting plasma glucose, respectively. As for total cholesterol, HDL cholesterol, and triglycerides, the standardization and quality control of the laboratory was carried out using the reference serum of the Center for Adult Disease in Osaka, which has undergone a quality control program with the Center for Disease Control in Atlanta, USA. The mean and standard deviations were within approved limits. The level of low-density lipoprotein (LDL) cholesterol was calculated from total cholesterol, HDL cholesterol, and triglycerides with the aid of Friedewald’s formula (LDL cholesterol=total cholesterol - HDL cholesterol - triglyceride/5)\textsuperscript{12}. Although LDL cholesterol estimation becomes less accurate if the triglyceride value is 400 mg/dl or more\textsuperscript{13}, all participants showed serum triglyceride level less than 400 mg/dl.

Data on alcohol intake and cigarette smoking were obtained by interview. An interviewer assessed the usual weekly intake of alcohol in units of ‘go’ (a traditional Japanese unit of measurement, by volume, corresponding to 23 g of ethanol), which were converted to grams of ethanol per day. One go is 180 ml of Sake (Japanese rice wine), and it corresponds to one bottle (663 ml) of beer, two single shots (75 ml) of whisky, or two glasses (180 ml) of wine. The questionnaire asked about smoking habits (never, past, or current smoker); past or current smokers were asked about the number of cigarettes smoked per day and the duration of smoking in years. In this study, past and never smokers were combined, and the current amount of cigarettes smoked was used in the analysis.

Subjects were classified as clinically obesity if they had BMI 26.4 kg/m\textsuperscript{2} or greater. Hypertension was defined as systolic blood pressure 140 mmHg or greater and/or diastolic blood pressure 90 mmHg or greater. Impaired fasting glucose (IFG) and type 2 diabetes were assessed with the current guidelines of the American Diabetes Association\textsuperscript{14}: a fasting plasma glucose level at least 110 but less than 126 mg/dl for IFG and a fasting plasma glucose level 126 mg/dl or more or current receipt of hypoglycemic medication for type 2 diabetes, because an oral glucose tolerance test was not performed in every subject. Hyperuricemia was defined as a uric acid level 8.0 mg/dl or greater or receipt of medications for hyperuricemia for males and as a uric acid level 6.0 mg/dl or greater for females.

Although clinical cutpoints based on NCEP guidelines were 200 mg/dl for triglycerides and 35 mg/dl for HDL cholesterol\textsuperscript{15}, we used the cutpoints of 150 mg/dl for triglycerides and 40 mg/dl for HDL cholesterol to estimate the bivariate distributions of triglycerides and HDL cholesterol, based on the guideline for diagnosis and treatment for hyperlipidemia in Japanese adults\textsuperscript{16}. The previous studies in the United States have suggested the adverse influence of triglycerides on other cardiovascular risk variables at a considerably lower cutpoint (100–150 mg/dl) of
Therefore, serum triglyceride levels for each sex were subdivided into quartiles to examine the adverse influence of triglycerides on other cardiovascular risk factor variables. Age- and sex-specific cutpoints of the 75th percentile for triglycerides and the 25th percentile for HDL cholesterol were also used as a measure of the prevalence of cardiovascular morbidity.

 Statistical analysis

The analysis of variance was used to compare the means of the groups. The analysis of covariance was also used to test sex-specific differences in triglyceride mean levels; age, BMI, cigarette smoking, and alcohol intake were included as covariates. Age-related changes in serum triglyceride levels and triglyceride-related changes in the levels of selected cardiovascular risk factor variables were tested by linear regression. Multiple regression analysis was performed separately in each sex group to examine an independent association of factors and their relative importance as determinants of serum triglyceride levels. The aforelisted covariates along with (model 2) or without (model l) HDL cholesterol were included as independent variables. Logistic regression analyses were used to evaluate the relations between serum triglyceride levels and the prevalence of obesity, hypertension, IFG or type 2 diabetes, or hyperuricemia. For tests of significance, the logarithm for the triglyceride (because of the non-gaussian distribution of the frequency for this variable) was used.

 Data analysis was performed with the SPSS/PC statistical package (Marija J. Norusis, SPSS Inc., Chicago, IL, USA). All reported p-values are two-tailed and a p-value of less than 0.05 was considered significant.

 Results

The geometric mean and selected percentiles of serum triglyceride levels by age and sex groups are presented in Table 1. Triglyceride levels were significantly higher in males than in females at each of the age group (P<0.001). The sex differences persisted after controlling for the covariates: age, BMI, cigarette smoking, and alcohol intake. Triglyceride levels showed a significant increasing trend with age among males (P<0.001), but did not among females (P=0.102).

Figure 1 shows the bivariate distributions of serum triglyceride and HDL cholesterol levels by sex. With the
cutpoints of 150 mg/dl for triglycerides and 40 mg/dl for HDL cholesterol, 86.1% of males displayed normal levels of both triglycerides (< 150 mg/dl) and HDL cholesterol (≥ 40 mg/dl), while 98.7% of females had normal values. In terms of conjoint trait of dyslipidemia, 3.1% and 0.2% of males and females displayed high triglycerides (≥150 mg/dl) in combination with low HDL cholesterol (<40 mg/dl), respectively. Based on the NCEP cutpoints\(^\text{15}\), 94.0 % and 99.4% of males and females showed normal levels of both triglycerides (< 200 mg/dl) and HDL cholesterol (> 35 mg/dl), respectively. Only 0.5% of males displayed high triglycerides in combination with low HDL cholesterol, while none of females fell in this category.

Table 2 shows the levels of selected cardiovascular risk variables by serum triglyceride levels and sex. In both sexes, BMI, daily alcohol consumption, diastolic blood pressure, LDL cholesterol level, and fasting plasma glucose level increased in a dose-dependent manner as triglyceride level increased. On the other hand, HDL cholesterol level showed a decreasing trend with an increase in triglycerides. The number of cigarettes smoked per day, systolic blood pressure, and uric acid level increased in a dose-dependent manner as triglyceride level increased among males, but did not among females.

Multiple regression analyses were carried out to investigate the associations of age, BMI, cigarette smoking, alcohol intake, systolic blood pressure, and levels of LDL cholesterol, HDL cholesterol, fasting plasma glucose, and uric acid with Log triglyceride levels (Table 3). Systolic blood pressure was used as an index of blood pressure in this model, because systolic blood pressure was closely associated with diastolic blood pressure (r=0.645, \(p<0.001\)). Independent and significant correlates with Log triglyceride levels were, in the order of relative importance (model 1): BMI, LDL cholesterol level, cigarette smoking, age, uric acid level, and systolic blood pressure for males; and LDL cholesterol level, uric acid level, and BMI for females. The cumulative percentages of variation for Log triglyceride levels were 26.3% for males and 10.9% for females. When HDL cholesterol was included in the model (model 2), it accounted for 11.3% and 3.9% of the variation in triglycerides for males and females, respectively.

The prevalence of obesity, hypertension, IFG or type 2 diabetes, and hyperuricemia in the study subjects are shown in Fig. 2 by sex, according to serum triglycerides and HDL cholesterol status. Individuals with age- and sex-specific triglyceride levels above the 75th percentile (equivalent to 82–116 mg/dl for males and 56–63 mg/dl for females) versus below this level increased the prevalence of obesity, hypertension, IFG or type 2 diabetes, and hyperuricemia in both sexes. Conjoint trait of triglyceride levels above the 75th percentile and HDL cholesterol levels below the 25th percentile (equivalent to 45–49 mg/dl for males and 58–63 mg/dl for females) further increased the prevalence of these

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**Table 2. Levels (mean ± SD) of selected cardiovascular risk factor variables by serum triglyceride levels and sex**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Males</th>
<th>Females</th>
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<tbody>
<tr>
<td></td>
<td>Serum triglyceride levels (mg/dl)</td>
<td>Serum triglyceride levels (mg/dl)</td>
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<tr>
<td></td>
<td>&lt;50 (n=399)</td>
<td>50–69 (n=451)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
<td>21.7 ± 2.2</td>
<td>22.1 ± 2.5</td>
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<tr>
<td>Smoking (cigarettes/day)</td>
<td>8.5 ± 11.6</td>
<td>10.8 ± 12.6</td>
</tr>
<tr>
<td>Alcohol intake (g/day of ethanol)</td>
<td>12.2 ± 12.5</td>
<td>14.9 ± 15.6</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg)</td>
<td>118.7 ± 12.1</td>
<td>119.8 ± 11.8</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg)</td>
<td>68.2 ± 9.1</td>
<td>69.5 ± 10.4</td>
</tr>
<tr>
<td>Low-density lipoprotein cholesterol (mg/dl)</td>
<td>91.7 ± 20.9</td>
<td>103.0 ± 24.3</td>
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<tr>
<td>High-density lipoprotein cholesterol (mg/dl)</td>
<td>62.6 ± 12.3</td>
<td>59.0 ± 11.3</td>
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<tr>
<td>Fasting plasma glucose (mg/dl)</td>
<td>83.7 ± 4.9</td>
<td>84.9 ± 5.1</td>
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<tr>
<td>Uric acid (mg/dl)</td>
<td>5.48 ± 1.07</td>
<td>5.57 ± 1.04</td>
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*  P<0.05, **  P<0.01, ***  P<0.001.
Overall, triglyceride levels above the 75th percentile increased the risk (odds ratio (OR)) for having obesity, hypertension, IFG or type 2 diabetes, and hyperuricemia by 2.9 (95% confidence interval (CI)=2.0–4.3), 1.7 (CI=1.1–2.9), 1.8 (CI =0.6–5.7), and 3.0 (CI=1.6–5.9), respectively. As for conjoint trait of dyslipidemia, triglyceride levels above the 75th percentile and HDL cholesterol levels below the 25th percentile, compared with triglyceride levels the 75th percentile or less and HDL cholesterol levels the 25th percentile or more, were associated with increased risk of obesity (OR=8.7, CI=5.8–12.9), hypertension (OR=2.2, CI=1.5–3.3), IFG or type 2 diabetes (OR=1.7, CI =0.5–5.2), and hyperuricemia (OR=6.0, CI=3.2–11.5). The respective ORs for triglyceride levels the 75th percentile or less and HDL cholesterol levels below the 25th percentile were 3.2 (CI=2.0–5.0), 1.2 (CI=0.7–2.0), 0.4 (CI=0.1–3.4), and 1.5 (CI=0.6–3.7), and those for triglyceride levels above the 75th percentile and HDL cholesterol levels the 25th percentile or more were 3.9 (CI=2.6–6.0), 1.5 (CI=0.9–2.6), 1.6 (CI=0.5–5.9), and 3.3 (CI=1.6–6.6).

**Discussion**

The present study demonstrates that serum triglyceride levels of a population-based sample of young Japanese adults vary markedly by sex and that the age-related increase in serum triglyceride levels was more pronounced in males. The sex (males > females) differences in serum triglycerides seen in the present study, which persisted after controlling
for age, BMI, cigarette smoking, and alcohol intake, are in agreement with earlier findings in this age group\(^3\), \(^10\), \(^11\). Based on common cutpoints, 9.4% and 0.8% of males and females had high triglyceride levels (≥ 150 mg/dl), respectively. In terms of conjoint trait of dyslipidemia, 86.1% of males displayed normal levels of both triglycerides (< 150 mg/dl) and HDL cholesterol (≥ 40 mg/dl), while 98.7% of females had normal values. Only 3.1% and 0.2% of males and females displayed high triglycerides in combination with low HDL cholesterol. These results demonstrate that young Japanese adults mostly have normal lipid profiles relating to serum triglycerides and HDL cholesterol status with common cutpoints of serum lipid and lipoprotein.

A high serum triglyceride level is markers for raised concentrations of atherogenic triglyceride-rich lipoproteins, abnormally small particles of LDL, and low serum concentrations of HDL, and the combination of high serum triglyceride levels, small LDL particles, and low HDL cholesterol levels has been named the atherogenic lipoprotein phenotype\(^17\)–\(^19\), or simply, the lipid triad. Moreover, since high triglyceride levels commonly associate with other nonlipid risk phenotypes such as hypertension, insulin resistance, hyperuricemia, and a prothrombotic state\(^19\)–\(^27\), the clustering of these nonlipid risk factors along with the lipid triad has been called the metabolic syndrome\(^19\). Furthermore, cigarette smoking increases beta lipoproteins, and this effect is secondary to the higher very low density lipoprotein (VLDL) triglyceride levels in whole serum and this effect is secondary to the higher very low density lipoprotein (VLDL) triglyceride levels in whole serum and a VLDL fraction in smokers\(^29\). The rise in serum triglycerides caused by alcohol is mainly due to increased synthesis of triglycerides in VLDL\(^29\), \(^30\).

There is the abundant evidence that serum triglycerides independently predict initial CHD events\(^1\)–\(^3\), \(^5\), \(^6\), \(^31\)–\(^36\), and mild to moderately elevated levels generally considered as normal are associated with CHD risk\(^5\)–\(^6\), \(^35\), \(^36\). Atherogenic lipoprotein phenotype, i.e. a combination of triglyceride-rich lipoproteins, small LDL particles and low HDL cholesterol\(^17\)–\(^19\), has been found to become prevalent even at triglyceride levels of 100–150 mg/dl\(^18\), \(^24\), and it is increasingly being recognized that the level of fasting serum triglycerides (< 200 mg/dl) currently viewed as desirable may be too high\(^2\)–\(^8\). In this study, age, BMI, cigarette smoking, alcohol intake, systolic and diastolic blood pressures, and levels of LDL cholesterol, HDL cholesterol (negative), fasting plasma glucose, and uric acid were associated with triglyceride levels in the expected directions, and adverse profiles of aforesaid risk variables were observed at serum triglyceride levels considered as normal (< 150 mg/dl). As for cardiovascular morbidity, individuals with sex-, and age-specific triglyceride levels above the 75th percentile (equivalent to 82–116 mg/dl for males and 56–63 mg/dl for females) displayed increased prevalence of obesity, hypertension, and hyperuricemia, and conjoint trait of triglyceride levels above the 75th percentile and HDL cholesterol below the 25th percentile (equivalent to 45–49 mg/dl for males and 58–63 mg/dl for females) further increased the prevalence of these conditions. These results indicate that serum triglyceride levels generally considered as normal have a threshold effect on cardiovascular risk in young Japanese adults and that these tendencies are more pronounced among those with low HDL cholesterol levels. Considerations of lowering a cutpoint for serum triglycerides may be needed in terms of cardiovascular risk assessment during young adulthood.

In summary, our results show that serum triglycerides at levels considered as normal were adversely related to cardiovascular risk variables in healthy young Japanese adults. Control of modifiable risk factors such as obesity, cigarette smoking, and alcohol intake provides a rational approach to prevention of risk associated with even moderately elevated serum triglyceride levels.

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**References**

5. Castelli WP (1992) Epidemiology of triglycerides: a
view from Framingham. Am J Cardiol 70, 3H–9H.


