Lower the triglyceride, longer the survival

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ABSTRACT

Background: We tried to determine the safest triglyceride value in the plasma.

Methods: Check up cases with a triglyceride value lower than 60 mg/dL were collected into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and equal to or greater than 200 mg/dL into the fifth groups, respectively.

Results: Study included 478 cases (288 females and 190 males), totally. Mean values of age, body weight, body mass index, triglyceride, and low density lipoprotein cholesterol and prevalences of smoking, white coat hypertension (WCH), hypertension, type 2 diabetes mellitus (DM), and coronary artery disease (CAD) increased nearly in all steps from the first towards the fifth groups, gradually and significantly (p<0.05).

Conclusions: Probably metabolic syndrome is a chronic inflammatory process mainly affecting the vascular endothelium all over the body and terminating with early aging and premature death. The syndrome has reversible parameters including sedentary lifestyle, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbeta-lipoproteinemia, dyslipidemia, impaired fasting glucose, impaired glucose tolerance, WCH, chronic inflammations and infections and irreversible end points including obesity, hypertension, DM, cirrhosis, peripheral artery disease, chronic obstructive pulmonary disease, chronic renal disease, CAD, mesenteric ischemia, osteoporosis, and stroke. Hypertriglyceridemia may be one of the most significant reversible parameters of the syndrome, and it is better to have the lowest plasma triglyceride value as much as possible to live longer.

Key words: Triglyceride, metabolic syndrome, atherosclerosis, early aging, premature death
Introduction

Chronic endothelial damage may be the most common kind of vasculitis and the leading cause of aging, morbidity, and mortality in human beings (1-4). Much higher blood pressure (BP) of the afferent vasculature may be the major underlying cause by inducing recurrent injuries on endothelium, and probably whole afferent vasculature including capillaries are involved in the process. Thus the term of venosclerosis is not as famous as atherosclerosis in the literature. Secondary to the chronic endothelial inflammation, edema, and fibrosis, vascular walls become thickened, their lumens are narrowed, and they lose their elastic natures that reduce blood flow to terminal organs and increase systolic BP further. Some of the well-known causes and indicators of the inflammatory process are sedentary lifestyle, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, impaired fasting glucose (IFG), impaired glucose tolerance (IGT), white coat hypertension (WCH), and chronic inflammatory processes including rheumatologic disorders, chronic infections, and cancers for the development of terminal complications including obesity, hypertension, diabetes mellitus (DM), cirrhosis, peripheral artery disease (PAD), chronic obstructive pulmonary disease (COPD), chronic renal disease (CRD), coronary artery disease (CAD), mesenteric ischemia, osteoporosis, and stroke, all of which terminate with early aging and premature death (5-9). Although early withdrawal of causative factors may prevent irreversible complications, after development of cirrhosis, COPD, CRD, CAD, PAD, or stroke, endothelial changes cannot be reversed completely due to their fibrotic nature. The accelerator factors and terminal consequences were researched under the titles of metabolic syndrome, aging syndrome, or accelerated endothelial damage syndrome in the literature, extensively (10-13). On the other hand, although its normal limits could not be determined clearly yet, hypertriglyceridemia is one of the significant indicators of the metabolic syndrome (14). Due to the growing evidence for a strong association between increased plasma triglyceride values and prevalence of CAD, Adult Treatment Panel (ATP) III adopts lower cutpoints for triglyceride abnormalities than did ATP II (15, 16). Although ATP II determined the normal triglyceride value as lower than 200 mg/dL in 1994, World Health Organisation (WHO) in 1999 (17) and ATP III in 2001 reduced its normal limit as lower than 150 mg/dL (15). Although these cutpoints are usually used to define limits of the metabolic syndrome, there are suspicions about the safest limits of plasma triglyceride values in the literature. We tried to determine the safest triglyceride value in the plasma.

Material and methods

The study was performed in the Internal Medicine Polyclinic of the Medical Faculty of the Dumlupinar University on routine check up patients between August 2005 and March 2007. Consecutive patients between the ages of 15 and 70 years were studied to prevent debility induced weight loss in elders. Their medical histories including hypertension, DM, dyslipidemia, and already used medications were learnt, and a routine check up procedure including an electrocardiography, fasting plasma glucose (FPG), triglyceride, and low density lipoprotein cho-

lesterol (LDL-C) was performed. Current daily smokers, at least with six pack-months, and cases with a history of five pack-years were accepted as smokers. Patients with devastating illnesses including type 1 DM, malignancies, acute or chronic renal failure, chronic liver diseases, hyper-or hypothyroidism, and heart failure were excluded to avoid their possible effects on weight. Additionally, anti-hyperlipidemic drugs or metformin users were excluded to avoid their possible effects on blood lipid profile (18). Body mass index (BMI) of each case was calculated by the measurements of the same physician instead of verbal expressions. Weight in kilograms is divided by height in meters squared (15). Cases with an overnight FPG level of 126 mg/dL or greater on two occasions or already receiving antidiabetic medications were defined as diabetics (15). An oral glucose tolerance test with 75-gram glucose was performed in cases with a FPG level between 110 and 126 mg/dL, and diagnosis of cases with a 2-hour plasma glucose level of 200 mg/dL or greater is DM (15). Additionally, office blood pressure (OBP) was checked after a 5 minute rest in seated position with a mercury sphygmomanometer on three visits, and no smoking was permitted during the previous 2 hours. A 10-day twice daily measurement of blood pressure at home (HBP) was obtained in all cases, even in normotensives in the office due to the risk of masked hypertension after a 10-minute education session about proper BP measurement techniques (19). An additional 24-hour ambulatory blood pressure monitoring (ABP) was obtained just in cases with a higher OBP and/or HBP measurement. It was performed with oscillometrical equipment (SpaceLabs 90207, Redmond, Washington, USA) set to take a reading every 10 minutes throughout the 24 hours. Eventually, hypertension is defined as a BP of 135/85 mmHg or greater on mean daytime (between 10 AM to 8 PM) ABP, WCH as an OBP of 140/90 mmHg or greater but mean daytime ABP of <135/85 mmHg (19). A stress electrocardiography was performed just in suspected cases as a result of the routine electrocardiography, and a coronary angiography was obtained just for the stress electrocardiography positive cases. Eventually, patients with a triglyceride value lower than 60 mg/dL were collected into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and equal to or greater than 200 mg/dL into the fifth groups, respectively. The female ratio, values of the mean age, weight, BMI, triglyceride, and LDL-C, and prevalences of smoking, WCH, hypertension, DM, and CAD were detected in each group and compared. Mann-Whitney U test, Independent-Samples T test, and comparison of proportions were used as the methods of statistical analyses.

Results

The study included 478 cases (288 females and 190 males), totally. The mean ages of the groups increased up to the triglyceride value of 200 mg/dL, significantly (p<0.05 in all steps), then decreased nonsignificantly (50.5 versus 48.6 years, p>0.05). There were 117 smokers totally, and only 27.3% (32) of them were females. On the other hand, prevalence of smoking was the highest in the highest triglyceride value having group. The mean body weight increased continuously, parallel to the increasing value of triglyceride, whereas BMI increased up to the triglyceride value of 200 mg/dL, and then decreased. Similarly, the mean LDL-C reached its the highest value in the fourth,
Table 1: Characteristics of the study cases

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
<th>Mean ± SD</th>
<th>p-value</th>
<th>ns</th>
<th>(\hat{p})-value</th>
<th>(\hat{p})-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG value lower than 200 mg/dL</td>
<td>86</td>
<td>48.6 ± 10.9</td>
<td>0.002</td>
<td>ns</td>
<td>47.6% (41)</td>
<td>45.5% (40)</td>
</tr>
<tr>
<td>TG value lower than 150 mg/dL</td>
<td>87</td>
<td>50.5 ± 11.2</td>
<td>0.0002</td>
<td>ns</td>
<td>56.3% (49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TG value lower than 100 mg/dL</td>
<td>125</td>
<td>59.4 ± 12.9</td>
<td>0.001</td>
<td>ns</td>
<td>60.8% (76)</td>
<td>26.4% (23)</td>
</tr>
<tr>
<td>TG value lower than 60 mg/dL</td>
<td>122</td>
<td>44.8 ± 13.8</td>
<td>0.0019</td>
<td>ns</td>
<td>65.5% (80)</td>
<td>23.0% (29)</td>
</tr>
<tr>
<td>TG value lower than 30 mg/dL</td>
<td>122</td>
<td>44.8 ± 13.8</td>
<td>0.0019</td>
<td>ns</td>
<td>65.5% (80)</td>
<td>23.0% (29)</td>
</tr>
</tbody>
</table>

*Triglyceride
†Nonsignificant (p>0.05)
‡Body mass index
§Low density lipoprotein cholesterol.
Excess weight leads to both structural and functional abnormalities of many systems of the body. Recent studies revealed that adipose tissue produces leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, adiponectin, and other cytokines which act as acute phase reactants in the plasma (20, 21). For example, the cardiovascular field has recently shown a great interest in the role of inflammation in the development of atherosclerosis and numerous studies indicated that inflammation plays a significant role in the pathogenesis of atherosclerosis and thrombosis (1, 2). On the other hand, individuals with excess weight have an increased blood volume as well as an increased cardiac output thought to be the result of increased oxygen demand of the excessive fat tissue. The prolonged increase in blood volume can lead to myocardial hypertrophy and decreased compliance in addition to the common comorbidity of hypertension. In addition to them, the prevalences of high FPG, high serum total cholesterol, and low high density lipoprotein cholesterol (HDL-C) increased parallel to the higher BMI values (22). Combination of these cardiovascular risk factors will eventually lead to an increase in left ventricular stroke work with higher risks of arrhythmias, cardiac failure, and sudden cardiac death. Similarly, the prevalences of CAD and stroke increased parallel with the higher BMI values in some other studies (22, 23), and risk of death from all causes including cancers increased throughout the range of moderate to severe weight excess in all age groups (24). The relationships between excess weight and elevated BP and hypertriglyceridemia were described in the metabolic syndrome (14), and clinical manifestations of the syndrome included obesity, dyslipidemia, hypertension, insulin resistance, and proinflammatory and prothrombotic states (12). Similarly, prevalences of smoking (42.2% versus 28.4%, p<0.01), excess weight (83.6% versus 70.6%, p<0.01), DM (16.3% versus 10.3%, p<0.05), and hypertension (23.2% versus 11.2%, p<0.001) were all higher in the hypertriglyceridemia cases in another study (25). It is a well-known fact that smoking causes a chronic inflammatory process in the respiratory tract, lungs, and vascular endothelium all over the body terminating with an accelerated atherosclerosis, end-organ insufficiencies, early aging, and premature death thus it should be included among the major parameters of the metabolic syndrome. On the other hand, smoking-induced weight loss is probably related with the smoking-induced endothelial inflammation all over the body since loss of appetite is one of the main symptoms of disseminated inflammation in the body. In another explanation, smoking-induced loss of appetite is an indicator of being ill instead of being healthy during smoking (26-28). Buerger’s disease (thromboangiitis obliterans) alone is also a clear evidence to show the strong atherosclerotic effects of smoking since this disease has not been shown in the absence of smoking up to now. On the other hand, the prevalences of hyperbetalipoproteinemia were similar in the hypertriglyceridemia and control groups (18.9% versus 16.3%, p>0.05, respectively) in the above study (25).
Although ATP II determined the normal triglyceride value as lower than 200 mg/dL in 1994 (16), WHO in 1999 (17) and ATP III in 2001 (15) reduced this normal limit as lower than 150 mg/dL. Although these cutpoints are usually used to define limits of the metabolic syndrome, whether or not more lower limits provide additional benefits for human beings is unclear. In the present study, patients with a triglyceride value lower than 60 mg/dL were collected into the first, lower than 100 mg/dL into the second, lower than 150 mg/dL into the third, lower than 200 mg/dL into the fourth, and equal to or greater than 200 mg/dL were collected into the fifth groups, respectively. Prevalence of smoking was the highest in the fifth group which may also indicate inflammatory roles of smoking and hypertriglyceridemia in the metabolic syndrome. The mean body weight increased continuously, parallel to the increasing value of triglyceride. As the most surprising result, the prevalences of hypertension, type 2 DM, and CAD, as some of the terminal end points of the metabolic syndrome, showed their most significant increases after the triglyceride value of 100 mg/dL. As of our opinion, significantly increased mean age by the increased triglyceride values may be secondary to aging induced decreased physical and mental stresses, which eventually terminates with onset of excess weight and other parameters and terminal end points of the metabolic syndrome. Interestingly, although the mean age increased from the lowest triglyceride having group towards the triglyceride value of 200 mg/dL, then decreased. The similar trend was also seen in the mean LDL-C and BMI values, and prevalence of WCH. These trends may be due to the fact that although the borderline high triglyceride values (150-199 mg/dL) are seen together with overweight, obesity, physical inactivity, smoking, and alcohol like acquired causes, the high triglyceride (200-499 mg/dL) and very high triglyceride values (500 mg/dL and higher) are usually secondary to both acquired and secondary causes such as type 2 DM, chronic renal failure, and genetic patterns (15). But although the underlying causes of the high and very high triglyceride values may be a little bit different, probably risks of the terminal end points of the metabolic syndrome do not change in these groups, too. For example, prevalences of hypertension and type 2 DM were the highest in the highest triglyceride value having group in the present study. Eventually, although some authors reported that lipid assessment in vascular disease can be simplified by measurement of either total and HDL-C levels without the need of triglyceride (29), the present study and most others indicated a causal association between triglyceride-mediated pathways and parameters of the metabolic syndrome (30). Similarly, another study indicated moderate and highly significant associations between triglyceride values and CAD in Western populations (31).

As a conclusion, probably metabolic syndrome is a chronic inflammatory process mainly affecting the vascular endothelium all over the body and terminating with early aging and premature death. The syndrome has reversible parameters including sedentary life style, animal-rich diet, overweight, smoking, alcohol, hypertriglyceridemia, hyperbetalipoproteinemia, dyslipidemia, IFG, IGT, WCH, chronic inflammations and infections and irreversible end points including obesity, hypertension, DM, cirrhosis, PAD, COPD, CRD, CAD, mesenteric ischemia, osteoporosis, and stroke. Hypertriglyceridemia may be one of the most significant reversible parameters of the syndrome, and it is better to have the lowest plasma triglyceride value as much as possible to live longer.

References


