Lipid disorders and their changes in postsocialist Estonia

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The aim of the study was to investigate the time trends of total cholesterol (TC) and triglycerides (Tg) concentration in blood plasma in inhabitants of Tallinn and to assess the predictive power of these lipids for mortality.

Two independent random samples of the population of Tallinn aged 30 to 54 were examined in 1984–1987 and in 1992–1994. TC and Tg were determined in 1747 men and 561 women at the first survey and 292 men and 162 women at the second survey. The lipid profile was assessed by the EAS classification of hyperlipidaemia.

The proportion of individuals with normal lipid values (TC and Tg both below 200 mg/dl) increased from the I to the II survey (from 30.1 % to 38.2 % in men and from 28.6 % to 47.9 % in women). The percentage of men belonging to group A decreased from 40.0 to 30.7 % and of women from 44.1 to 34.0 %. The prevalence of most severe forms of hyperlipidaemia did not change significantly (group D + E was observed in 12.3 % of men at the I survey and in 9.7 % at the II survey; the corresponding figures for women were 8.8 % and 8.9 %). Between the I and II survey Tg mean values decreased in men aged 30 to 54 and TC mean values decreased in women of the same age-group.

According to this study nearly 100,000 inhabitants of Estonia aged 20 to 70 need pharmacological treatment, more than 500,000 need nonpharmacological correction of hyperlipidaemia. By means of quantile analysis and Cox regression model TC and Tg were determined in subsamples comprising 1747 men and 561 women at the I survey and 292 men and 162 women at the II survey. Thus, the proportion of male participants in whom lipids were measured was 92 % at the I survey and 39 % at the II survey; the corresponding figures for females were 66 % and 29 %.

At both surveys the screening procedure included standard epidemiological investigation methods: blood pressure, height and weight measurements, determination of TC and Tg; ECG at rest classified according to the Minnesota Code. The questionnaire collected data on smoking, alcohol consumption, education, occupation, ethnic origin, marital status; the Rose questionnaire was used for determination of angina at effort. The classification of the CHD status was as follows: possible CHD-Minnesota Code classes 1.2.8–1.3; 4.3; 5.3; 4.1.2 and 5.1.2 together with 3.1 or 3.3; 6.1; 7.1; 8.3; history of possible myocardial infarction according to the cardiovascular questionnaire; definite CHD-Minnesota Code classes 1.1–1.2.7; 4.1.2; 5.1.2 without 3.1 or 3.3; angina by Rose. The subjects were asked to fast at least 12 h before the blood test. The 12 to 14 fasting TC [13] and Tg [14] were determined using a Centrifihem-600 autoanalyzer. The screening procedure has been described in more detail elsewhere [15, 16]. Measurements were performed by the same team which underwent a similar training and standardization procedure for both surveys.

The lipid profile was assessed by TC and Tg mean values as well as by the EAS classification of hyperlipidaemia [17]. According to the above mentioned classification, 5 groups were identified as follows. A (mild hypercholesterolaemia): TC 200–250 mg/dl, Tg < 200 mg/dl; B (moderate hypercholesterolaemia): TC 250–300 mg/dl, Tg < 200 mg/dl; C (isolated hypertriglyceridaemia): TC < 200 mg/dl, Tg 200–500 mg/dl; D (mixed form): TC 200–300 mg/dl, Tg 200–500 mg/dl; E (severe hypercholesterolaemia and/or hypertriglyceridaemia): TC > 300 mg/dl and/or Tg > 500 mg/dl.

Two groups of men residing in Tallinn, aged 30 to 59, who underwent initial epidemiological examinations in 1981/82

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and 1984/85, accordingly, were subject to a follow-up study. The group of the first survey (2177 men) was followed up during 12 years in average (26292 person-years) and the group of the second survey (1833 men) for 9.8 years (18586 person-years); thus 4,070 men in total were followed up during 11 years in average (44878 person-years). During the follow-up period the endpoints (all deaths) of men born in corresponding years were registered at the Registry Office every month, and the death cases of the participants were identified according to these data. The life status of the rest of the group was also verified by the end of the follow-up period at the Address Office and by personal contact by mail. The causes of death were verified by an expert committee according to death certificates and medical records by means of WHO criteria [18]. Death cause was classified according to ICD-IX classification. Pooled data of both groups were used in this study.

The relationship between lipids and mortality from CHD, cerebrovascular disease, all cardiovascular diseases, oncologic diseases, external causes and all causes was studied by means of quantile analysis: the age-adjusted mortality rates from different causes of death were analyzed according to quintiles of TC and Tg. The risk ratio (RR) was determined as relationship between age-adjusted mortality in the highest and lowest risk categories.

The Cox proportional hazards regression model [19] was used to determine the predictive power of TC, Tg and other factors: CHD at entry, systolic blood pressure, diastolic blood pressure, heart rate, body mass index, alcohol (g/ethanol taken usually and during last week), education, occupation, marital status, ethnic origin.

The advantage of the Cox model, in comparison to multiple logistic estimation [20], is the possibility to take into account the time factor. The input of the variables is reflected by the Wald Chi Square which is calculated as:

$$\beta_{\text{stand}}^2 = \left( \frac{\beta}{\text{SE}} \right)^2$$

where $\beta$ is the regression coefficient of a given variable and SE is its standard error.

The data were analyzed using the SAS [21]. The methodology of this analysis has been described in more details elsewhere [22].

Figure 1. Distribution of the population of Tallinn aged 30 to 54 according to the EAS classification of hyperlipidaemia at the I survey

Figure 2. Distribution of the population of Tallinn aged 30 to 54 according to the EAS classification of hyperlipidaemia at the II survey. EAS – European Atherosclerosis Society
**Results**

Figure 1 demonstrates that at the first survey 30.1% of men and 28.6% of women aged 30 to 54 had TC and Tg values below 200 mg/dl; 40.0% of men and 44.1% of women belonged to group A (TC 200–250 mg/dl). TC 250–300 mg/dl (gr. B) was found in 16.7% of men and 9.2% of women. Isolated hypertriglyceridaemia was observed very seldom (0.9% of men and 0.1% of women). The prevalence of mixed hyperlipidaemia forms (D+E) was 12.3% in men and 8.8% in women. At the second survey (figure 2) the proportion of individuals with normal lipid values increased, it was more pronounced in women (47.9% vs 28.6%) than in men (38.2 vs 30.1). The proportion of individuals belonging to group A decreased in men from 40.0 to 30.7% and in women from 44.1 to 34.0%. The prevalence of the most severe forms of hyperlipidaemia did not change significantly.

From the first to the second survey the proportion of individuals with elevated TC values (> 200 mg/dl) decreased from 69.1 to 61.4% in men and from 71.3 to 52.1% in women. The percentage of men with elevated Tg values (> 200 mg/dl) was also lower at the second survey than at the first survey (4.5% vs 10.1%).

At the second survey the TC mean values in men aged 50 to 54 and the Tg mean values in men aged 40 to 54 were significantly lower in comparison to the values in similar age groups at the first survey (table 1). The age-adjusted Tg mean values decreased between the first and the second survey in the total group of men aged 30 to 54 from 115.5 mg/dl to 100.8 mg/dl (p < 0.05).

At the second survey women aged 30 to 49 had lower TC mean values than at the first survey; the age-adjusted TC mean values in women aged 30 to 54 decreased between the first and the second survey from 228.1 mg/dl to 207.8 (p < 0.05). No significant changes were observed in Tg mean values in women between the first and the second survey.

Along with this trends in serum lipids a decrease in mean values of systolic blood pressure, diastolic blood pressure and body mass index was observed, while the percentage of daily smokers increased, both in men and women (table 2).

During the 11-years follow-up of the male group 457 death cases were registered. The age-adjusted mortality rates from different causes of death were analyzed according to quintiles of TC and Tg. TC quintiles were as follows: I quintile < 190 mg/dl; II quintile 191–212 mg/dl; III quintile 213–233 mg/dl; IV quintile 234–260 mg/dl; V quintile > 260 mg/dl. Tg quintiles were: I quintile < 69 mg/dl; II quintile 69–87 mg/dl; III quintile 88–110 mg/dl; IV quintile 111–152 mg/dl; V quintile > 152 mg/dl.

The relationships between TC, Tg and mortality rates from different causes are shown in figures 3 and 4. The RR: age-adjusted CHD mortality rate in the top quintile of the TC distribution (3.48 ± 0.76 deaths per 1,000 person/years)
According to the Cox proportional hazards model, the Wald Chi-square where TC holds the sixth place after CHD for CHD mortality placed in rank order according to their model TC was found predictive only for CHD mortality. Trends were found for CHD mortality.

In the II quintile 2.8-fold (statistically insignificant). Similar tendencies were the highest in the V quintile of Tg exceeding those in years); p < 0.05. All cardiovascular diseases mortality rates than in the II quintile (0.57 ± 0.26 deaths per 1,000 person/years) vs bottom quintile (1.61 ± 0.43 deaths per 1,000 person/years) was 2.2 (p < 0.05). None of the other causes of death were related to TC values. Nevertheless, certain tendencies were observed which were different for the individual causes of death. For instance, there was a tendency to a higher mortality rate for all cardiovascular diseases in the top quintile and higher cancer mortality rates in the bottom quintile of TC distribution (statistically insignificant). The relationship between TC and total mortality was U-shaped.

In the V quintile of the Tg distribution the age-adjusted cerebrovascular mortality rates (2.4 ± 0.75 deaths per 1,000 person/years) were 3.4 times higher than in the I quintile (0.71 ± 0.4 deaths per 1,000 person/years) and 4.2 times higher than in the II quintile (0.57 ± 0.26 deaths per 1,000 person/years); p < 0.05. All cardiovascular diseases mortality rates were the highest in the V quintile of Tg exceeding those in the II quintile 2.8-fold (statistically insignificant). Similar tendencies were found for CHD mortality.

According to the Cox proportional hazards regression model TC was found predictive only for CHD mortality. Table 3 demonstrates the variables which were found predictive for CHD mortality placed in rank order according to their Wald Chi-square, where TC holds the sixth place after CHD status at entry, age, systolic blood pressure, smoking status and occupation (blue collar work).

None of the analyzed causes of death were related to Tg according to the Cox proportional hazards model.

### Discussion

Epidemiological studies performed on inhabitants of Tallinn in the mid of the 1980s confirmed the results of previous investigations which showed high TC values in inhabitants of Estonia [23–25]. The TC mean values in men residing in Tallinn are higher than in inhabitants of the other cities in the former USSR [26], the United States [27], Eastern and Southern Europe; they are similar to those in Western European populations, but somewhat lower than in Northern Europe [28]. The TC mean values in female inhabitants of Tallinn are also approximately similar to the average in women residing in Western European countries, higher than in their counterparts in Southern Europe and the United States and lower than in Northern and Eastern Europe [27, 28]. The Tg mean values in residents of Tallinn are almost similar as the Estonian Population Register was formed similar as the Estonian Population Register was formed on the basis of lists of electors. The only factor which could influence the results of the second survey to some extent is the lower response rate, as nonresponders are known as having higher levels of risk factors than responders [29]. From this point of view we could expect similar time trends of all the risk factors which would have been lower at the second survey than at the first one. In our study the time trends of the individual risk factors were different: lipids, blood pressure and body mass index mean values decreased while smoking rates increased. These changes in nonlipid risk factors are described by us in more detail elsewhere [30–32]. Anyway, the lower response rate at the second survey should be taken into consideration as a possible cause for bias.

Favourable changes in lipids as well as in body mass and blood pressure can be explained by favourable nutrition changes during the observation period. Among the participants of the second survey 39.9 % reported having changed their dietary habits during the last 12 months: 23.9 % had switched from animal to vegetable fat, 23.9 % had used less fat and 17.1 % less sugar [33]. The improvement of dietary pattern was also found by means of the 24-hour recall method: the energy, fat, saturated fatty acids and cholesterol consumption decreased while the P/S ratio increased [34, 35]. Different trends in TC and Tg levels in men can be explained by different changes in diet which were more pronounced in certain age groups. A more detailed analysis on the connection between diet and lipid level trends in the male population was published elsewhere [35]. We suppose that an increase in alcohol consumption was the main reason why, despite favourable nutrition changes, Tg did not decrease in women while TC decreased (unpublished data). It might be supposed that the influence of the dietary factor upon lipids is partly realized through body mass which is a well known common correlate for lipids and blood pressure [15, 36, 37].

Analysing the reasons for the favourable nutrition changes we would like to stress at least three factors. Tremendous political, social and economical changes occurred in Estonia in the early 90s when the last survey was carried out. On the one hand, due to the development of a market economy, the possibility of a more rational and healthy food choice became a reality. On the other hand, the income and the purchasing power of a considerable part of the population decreased and that caused a decrease in consumption of traditional Estonian food, like pork and dairy products, rich in saturated fat and cholesterol. Thus, the socio-economical situation worked towards the main principles of healthy lifestyle which were the cornerstones of nation-wide preventive projects launched at that time in Estonia, for instance the Heart Project.

Despite certain favourable trends in the lipid profile of the population of Tallinn during the last 10 years, hyperlipidaemia is still prevalent in residents of Tallinn, Estonia: 7/3 of the male population and more than ½ of the female population aged

### Table 3.

Cox regression model for coronary heart disease mortality (3434 men aged 35 to 59 followed up for 11 years)

<table>
<thead>
<tr>
<th>Variable</th>
<th>β-coefficient</th>
<th>SE</th>
<th>Wald Chi-square</th>
<th>p</th>
<th>Risk ratio</th>
<th>95% confidence limit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs of CHD at entry</td>
<td>1.050906</td>
<td>0.23186</td>
<td>20.54445</td>
<td>0.0001</td>
<td>2.860</td>
<td>1.816 4.506</td>
</tr>
<tr>
<td>Age</td>
<td>0.062541</td>
<td>0.01666</td>
<td>14.09386</td>
<td>0.0002</td>
<td>1.065</td>
<td>1.030 1.100</td>
</tr>
<tr>
<td>Systolic blood pressure</td>
<td>0.012656</td>
<td>0.00385</td>
<td>10.81820</td>
<td>0.0010</td>
<td>1.013</td>
<td>1.005 1.020</td>
</tr>
<tr>
<td>Smoking status</td>
<td>0.585091</td>
<td>0.20244</td>
<td>8.35364</td>
<td>0.0038</td>
<td>1.7795</td>
<td>1.207 2.669</td>
</tr>
<tr>
<td>Blue collar work</td>
<td>0.418640</td>
<td>0.20205</td>
<td>4.29297</td>
<td>0.0383</td>
<td>1.520</td>
<td>1.520 2.258</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.004247</td>
<td>0.00217</td>
<td>3.84207</td>
<td>0.0500</td>
<td>1.004</td>
<td>1.000 1.0093</td>
</tr>
</tbody>
</table>
Lipid disorders in Estonia

30 to 54 have elevated lipid values (TC and/or Tg > 200 mg/dl). Assessing the distribution of the population according to the EAS classification of hyperlipidaemia we can assume that approximately 10% (groups D and E) are probably in need of pharmacological treatment. Applying these data to the entire population of Estonia aged 20 to 70 we can conclude that nearly 100,000 inhabitants of the country are potential users of antihyperlipidaemia drugs and 500,000 need nonpharmacological correction of hyperlipidaemia.

Data of this study confirm the predicting power of TC for CHD mortality in our population although, according to the Cox regression model, it is less pronounced than that of systolic blood pressure. Thus, our study does not support the hypothesis [38] that elevated cholesterol is the only risk factor for CHD and atherosclerosis. TC was not found predictive for cerebrovascular and all cardiovascular disease mortality in this study as, according to our previous publications [22, 39], was systolic blood pressure. The predictive power of Tg for cerebrovascular and all cardiovascular diseases mortality found by univariate analysis (quantile analysis) disappeared when multivariate analysis (Cox proportional hazards regression model) was performed.

Acknowledgement

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References

37. Roberts WC. Atherosclerotic risk factors – are there ten or is there only one. Am J Cardiol 1989, 64: 552–4.
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