A comparison of cardiovascular risk as measured by compound blood lipid indices and two indices including lifestyle factors in occupational health service

J. E. Berg
Department of Preventive Medicine, University of Oslo, PO Box 1130 Blindern, 0317 Oslo, Norway

Healthy employees in a non-manufacturing firm (n = 252) were divided into low and high cardiovascular risk subjects in order to compare different indices of cardiovascular risk for use in occupational health service. The levels of total cholesterol (TC), a compound index of blood lipid components, the 'atherogenic index' (ATH-index) defined as \( (TC-HDLc) \times [apoB]/(HDLc \times [apoA]) \), and two other compound indices, one Norwegian (Westlund) and one Scottish (Dundee score) were compared. Information on smoking habits and blood pressure were part of the two last indices. Cut-off values to separate between low and high risk subjects were defined with TC = 6.5mmol/l, HDLc = 0.9mmol/l, apoA = 1.8g/l and apoB = 1.3g/l, all values based on clinical guidelines in Norway. No smoking and a systolic blood pressure < 150mmHg was included as cut-off of the combined indices. According to the three indices (ATH, Westlund and Dundee) 102, 25 and 116 employees were allocated to the increased risk group. Persons allocated to the increased risk group by the combined indices and not by the compound index were practically all smokers. Systolic blood pressure differed between indices only for persons with extreme pressures. A compound blood lipid index of CV risk, which may be drawn easily in an occupational health setting in an unfasting state and sent by post to a laboratory, mimics the allocation of persons to an increased risk group using combined indices. Smokers with normal lipid values would be allocated to increased risk by the combined indices, but not necessarily by the compound index. The use of the compound index together with advice to stop smoking is suggested as a time-saving strategy.

Key words: Cardiovascular risk; prevention; smoking.

INTRODUCTION

Cardiovascular (CV) risk in employees may be evaluated using one of several existing instruments of screening and may be based on a plethora of risk factors such as blood pressure, blood clotting and lipid fractions, and societal factors such as smoking, diet, stress or environmental pollution. Serum total cholesterol (TC), smoking habits and blood pressure have been taken together in models for risk assessment. Such models including biological variables and societal variables cover some of the most important risk factors known to date, and have been based on prospective studies of population subgroups. Separately, the risk factors show strong correlations with later CV events at the epidemiological level, as established years ago. The performance of, for instance TC, in individual counselling however, has been ambiguous although many practitioners still rely to a great extent on TC measurements in clinical settings. In a Swedish study of management of hyperlipidemia, general practitioners, industrial medical officers and internists were compared to their use of tests of CV risk. TC tests were considered to be the most important indicator by 42%.
general practitioners, 23% of industrial medical officers and 26% of internists, whereas 46%, 63% and 56%, respectively, considered the LDL/HDLc-index test to be the best (LDL = low density lipoprotein). Prospective studies which have included HDLc indicate that TC/HDLc is a more superior measure of risk for coronary heart disease than TC or LDL levels.15

A significant difference between smokers and non-smokers has been observed in mortality studies from CV disease.15-20

In a similar way persons with high blood pressure run a greater risk of developing CV disease than normotensives.21-24 As a result of these observations several groups have tried to combine TC, blood pressure and smoking habits into one measure of CV risk.1,2 Based on prospective longitudinal studies both Westlund et al. and Tunstall-Pedoe et al. have developed an instrument using the above-mentioned three coronary risk factors. The former is based on a Norwegian sample of workers, and the latter on a Scottish factory worker population aged 40–59.

A compound blood lipid index has been proposed by Høstmark et al. which used TC, HDLc and apolipoproteins A-I and B (apoA and apoB, respectively).25,26 No blood lipid fraction measurements would be robust enough to adequately reflect smoking habit and diet. A compound index which would, albeit partly, reflect the underlying lifestyle factors, could be an improvement compared to the more complex indices of blood lipids and lifestyle factors.

**Compound blood lipid indices**

The relative amount of the apoB and cholesterol in low density lipoprotein (LDL) in blood can be different in CV disease cases and controls. As reported by Sniderman et al.27 patients may have hyper-betalipoproteinemina with fairly normal levels of total cholesterol. In line with this, it may be hypothesized that variations in the relative amounts of apoA and cholesterol in the antiatherogenic high density lipoproteins (HDLc) may also contribute to augment separation of patients and controls, when using compound indices as compared to TC.

It was previously shown that an atherogenic index (ATH-index), calculated as

\[
\text{ATH-index} = \frac{(\text{TC} - \text{HDLc}) \times \text{apoB}}{\text{apoA} \times \text{HDLc}}
\]

yielded better separation between angiographically defined coronary patients and controls than TC, TC/HDLc and other indices.25,26

The fractions involved in the atherogenic index may all be measured in non-fasting blood samples.28 This may be convenient for occupational health services and family doctors working in time-limited settings. Thus it would be of interest to compare the ability of such an atherogenic index to mimic the risk assessments done by the compound indices of Westlund and Tunstall-Pedoe.

**MATERIALS AND METHODS**

Fasting blood samples were collected by the author in 252 employees in a non-manufacturing firm in Oslo, Norway over a 1.5 year period as part of routine health examinations. Two persons refused blood tests and were omitted from the calculations. Methods of sampling and analysis, and coefficients of variation are given elsewhere.29 The employees recruited had no experience of coronary events, angina pectoris, stroke or renal disease. The following blood lipid fractions were determined for the present study: Total cholesterol (TC), high density lipoprotein cholesterol (HDLc), apolipoprotein A-I (apoA) and apolipoprotein B (apoB). Information on smoking habits (duration and quantity) was gathered during health examinations together with blood pressure measurement in the sitting position (Korotkoff's sound 1 for systolic [SBP] and sound 5 for diastolic blood pressure [DBP]).

A cut-off for this index has been proposed at 4.5 with TC = 6.5mmol/l, HDLc = 0.9mmol/l, apoA = 1.8g/l and apoB = 1.3g/l.29

The combined total cholesterol and blood pressure/smoking indices used in calculations were the Dundee coronary risk-disk index and Westlund's index. Dundee coronary risk-disk was developed during 1989–91 and was based on data from the United Kingdom Heart Disease Prevention Program. This cohort contained factory workers aged 40–59, initially investigated in 1971–73, and then followed-up for 5 years for non-fatal myocardial infarction and for coronary deaths. 5,203 men were studied, and 331 coronary events were observed. A multiple logistic function was calculated to give the 5-year risk of CHD event, Y, as follows:

\[
Y = \frac{1}{1+e^{-(a + b_1x_1 + b_2x_2 + b_3x_3)}}
\]

where a and b are constants and x1 = systolic blood pressure in mmHg, x2 = total cholesterol in mmol/l, and x3 = smoking code. The data of this study has been validated by data from the Whitehall study.30 The cut-off level used in the present study between normal and increased risk of coronary heart disease in the next five years was based on a nonsmoker with SBP = 150mmHg and a TC = 6.5 mmol/l. This is indicated by a Dundee score of 5.0.

Westlund and Nicolaysen used a Norwegian sample of 3,751 men aged 40–49 who were followed-up for ten years.2 The subjects for the study were collected from about 20 occupational health services in Oslo, Norway. During the ten-year follow-up 190 men died, of which 86 were coronary heart disease deaths (ICD-7 no. 420 + 782.4 + 795.2). The risk factors TC, systolic blood pressure and cigarette smoking were found to be roughly uncorrelated in the Oslo population. A discriminant function analysis using age, TC, SBP and
weight/height as predictor variables gave coefficients similar to those of the Framingham study. On the basis of a regression model the authors used TC, SBP, number of cigarettes smoked and sex as factors in a risk score calculation. A risk score ≥ 100 indicated a need for follow-up of the employee. A man with a SBP = 150mmHg, who was a nonsmoker and had a TC = 6.5mmol/l had a Westlund score of 33.75, which was the cut-off used in calculations in the present study. The Westlund index increases exponentially with the three risk factors. For instance, a 40 year old man smoking ten cigarettes a day, having a TC = 9.2mmol/l and a SBP of 166mmHg would have a total risk score of 400, whereas persons at no risk score below 10.

The statistical analysis was performed on a Macintosh computer using Statistica. Skewness and kurtosis was used as measures of spread. Correlation was used to test similarities between indices. Cluster analysis allowed us to test for groups of individuals with comparable risk measured by the indices. A significance level of 0.05 was chosen, if not otherwise indicated.

RESULTS

The age-distribution of the employees is shown in Figure 1 for men and women separately. Mean age was 40.2 years (SD = 11.5). There were 118 (46.8%) women. Figure 2 shows the distribution of the three indices, the atherogenic index (ATH-index), Westlund's Norwegian index (Westlund) and the Dundee coronary risk-disk index (Dundee). The skewness of the indices was 2.37, 4.62 and 2.91, whereas the kurtosis was 7.76, 25.10 and 15.45, respectively, thus rendering data not very suitable for factor analysis.

Based on the cut-off values described above, 102 (40.5%) employees were allocated to the increased risk group according to the ATH-index, 25 (9.9%) according to Westlund's index, and 116 (46.0%) according to the Dundee index. Fifty-three of the 252 employees had a TC ≥ 6.5mmol/l. Nine of these 53 had an ATH-index below 4.5 due to high HDLc and apolipoprotein A levels. Seven of these nine persons had a Dundee score above 5.0.

Figure 2. A matrix plot of index values from 252 employees according to ATH-index, Westlund and Dundee coronary risk-disk combined indices of cardiovascular risk. The figure gives frequency distribution in the left high to right low diagonal squares, and scatterplots of the three indices measured by the other two on each horizontal square. The dotted line indicates a simple regression line, and the solid lines the 95% confidence intervals. Numbers given on horizontal and vertical axis are the total scores of the ATH-index, Westlund and Dundee indices, respectively.

Table 1. Employees (n = 252) at increased risk of cardiovascular disease according to the compound indices of Westlund and Tunstall-Pedoe (Dundee risk-disk) not confirmed by the atherogenic index (ATH-index)

<table>
<thead>
<tr>
<th>Index</th>
<th>No. of employees not deemed at increased risk by the ATH-index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Westlund (≥ 33.75)</td>
<td>25 (all smokers)</td>
</tr>
<tr>
<td>Dundee (≥ 5.0)</td>
<td>116 (of whom 42 smokers, and the 3 remaining with high HDLc-values)</td>
</tr>
</tbody>
</table>

ATH-index = ([TC-HDLc] x [apoB]) / ([HDLc] x [apoA])

Table 2. Mean values of the ATH-index* and the compound indices of Westlund and Tunstall-Pedoe (Dundee risk-disk) in 252 employees in three clusters after K-means cluster analysis

<table>
<thead>
<tr>
<th>Index</th>
<th>Cluster 1 n = 8</th>
<th>Cluster 2 n = 47</th>
<th>Cluster 3 n = 197</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATH-index</td>
<td>15.6</td>
<td>8.0</td>
<td>3.7</td>
</tr>
<tr>
<td>Westlund</td>
<td>168.7</td>
<td>34.4</td>
<td>6.1</td>
</tr>
<tr>
<td>Dundee</td>
<td>21.4</td>
<td>9.8</td>
<td>4.4</td>
</tr>
</tbody>
</table>

ATH-index = ([TC-HDLc] x [apoB]) / ([HDLc] x [apoA])

Among the persons allocated by the ATH-index at increased risk we found 20 of the 25 employees deemed at increased risk by Westlund’s index, Table 1. The five persons not allocated in the increased risk category by the ATH-index were all smokers, one was hypertensive, and four of five had a Dundee score of more than 10.2.

One hundred and sixteen employees had a Dundee score ≥ 5.0, forty-five of whom were not captured by the ATH-index as increased risk persons. Of these 45 persons, 42 were smokers, and the remaining three all had a combination of both a high TC and HDLc-level. This last combination gave normal ATH-index values,
whereas the Dundee scores were elevated due to this index's disregard of HDLc-levels.

Casewise correlation between the 252 persons according to ATH-index and Dundee risk was 0.57 and between ATH-index and Westlund's index it was 0.51, whereas between ATH-index and TC/HDLc it was 0.95.

K-means cluster analysis of the three indices with three clusters resulted in 8, 47, and 197 persons in each cluster (Table 2). The first and second clusters with 55 employees (21.8%) had values on all indices indicating increased risk. Among the eight employees in cluster 1 only two had TC > 6.5, whereas in cluster 2, 12 of 47 employees had TC > 6.5.

Cluster analysis with age, sex and the three indices with three clusters gave 8, 48, and 196 cases in the clusters, respectively. The mean values of the indices were practically the same as indicated in Table 3. The largest cluster had the highest frequency of women.

**DISCUSSION**

No single risk factor would suffice in screening populations at risk of cardiovascular disease. Occupational health services in Norway have for decades routinely measured body mass index, blood pressure and total cholesterol, without using these data for comprehensive counselling on CV risk. Lifestyle factors such as smoking, diet and physical activity have also been employed, but not in a routine or reproducible way. The inadequacy of TC measurements at the individual level as a stand-alone method for cardiovascular risk assessment has prompted a search to incorporate either lifestyle factors (predominantly smoking habits) or new knowledge of lipid metabolism and atherosclerosis development into compound indices.

The correlation between the compound blood lipid factor index and the two different indices using TC, blood pressure and smoking quantity, was higher than expected when comparing such different indicators as blood lipid factors and elements of lifestyle. This may indicate that the number of false positive and negative values found by using TC alone as a guideline, may be partly overcome by either using lifestyle indicators as smoking and blood pressure as with the Westlund and Dundee scores, or by use of several blood lipid fractions indicating a balanced view of lipid transport in the body. The majority of employees not given an increased risk by the ATH-index alone (Table 1) were smokers, a fact which is very readily observed in the office of an occupational physician. The values given in Table 2 indicate that in some cases, i.e. in 13 out of 252 (5.2%), the combined indices suggest increased cardiovascular risk, although the lipid balance would be considered adequate. Using ATH-index values (Table 2) would reduce the possibility of false positive results leading to unnecessary restrictions in employees’ lifestyle.

The two clusters with increased risk according to all three indices (Table 3) accounted for 21.8% of employees, which is in keeping with levels found in 40-42 year old men and women in the general Norwegian population.

Although to date apolipoprotein levels in blood do not have an immediate correlate in changeable lifestyle factors, as between HDLc and smoking, the incorporation of them in compound indices may give CV risk evaluation a higher predictive value. Prospective studies including the compound indices may, however, be necessary to confirm this.

The components of the ATH-index may be measured in the nonfasting state, a great advantage in occupational and general practice settings. By using the same laboratory at every measurement, the higher coefficient of variation in apolipoprotein analysis than in TC analysis may be minimized. The higher price of ATH-index analysis compared to both TC/HDLc and TC analysis would be cost-effectively countered by the reduction in false positive and negative tests.

A time-conscious industrial medical officer would then be urged to use the ATH-index in connection with advice to stop smoking, as this probably is the most important risk factor for CV disease among workers.

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**Table 3.** Employees with serum total cholesterol > 6.5mmol/l, a low atherogenic index and an increased Westlund index or Dundee risk-disk score. 'S' after case-no. indicates a smoker.

<table>
<thead>
<tr>
<th>Case</th>
<th>TC mmol/l</th>
<th>HDLc mmol/l</th>
<th>ApoAg/l</th>
<th>ApoB/HDLc</th>
<th>ATH-ind</th>
<th>Dundee</th>
<th>Westlund</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 S</td>
<td>6.9</td>
<td>1.6</td>
<td>155</td>
<td>182</td>
<td>4.0</td>
<td>11.0</td>
<td>54.5</td>
</tr>
<tr>
<td>2 S</td>
<td>5.8</td>
<td>1.7</td>
<td>151</td>
<td>160</td>
<td>2.5</td>
<td>10.5</td>
<td>36.0</td>
</tr>
<tr>
<td>3 S</td>
<td>6.4</td>
<td>1.5</td>
<td>149</td>
<td>170</td>
<td>3.6</td>
<td>10.3</td>
<td>41.3</td>
</tr>
<tr>
<td>4 S</td>
<td>7.5</td>
<td>2.1</td>
<td>184</td>
<td>199</td>
<td>2.9</td>
<td>13.1</td>
<td>145.1</td>
</tr>
<tr>
<td>5 S</td>
<td>5.8</td>
<td>1.4</td>
<td>142</td>
<td>181</td>
<td>4.2</td>
<td>6.9</td>
<td>59.0</td>
</tr>
<tr>
<td>6</td>
<td>7.7</td>
<td>1.8</td>
<td>164</td>
<td>205</td>
<td>4.0</td>
<td>6.8</td>
<td>6.1</td>
</tr>
<tr>
<td>7 S</td>
<td>6.9</td>
<td>1.7</td>
<td>163</td>
<td>176</td>
<td>3.3</td>
<td>7.5</td>
<td>32.2</td>
</tr>
<tr>
<td>8</td>
<td>8.6</td>
<td>1.6</td>
<td>157</td>
<td>146</td>
<td>4.0</td>
<td>7.8</td>
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<tr>
<td>9 S</td>
<td>6.9</td>
<td>1.6</td>
<td>155</td>
<td>182</td>
<td>4.0</td>
<td>11.0</td>
<td>54.5</td>
</tr>
<tr>
<td>10</td>
<td>6.7</td>
<td>1.1</td>
<td>137</td>
<td>114</td>
<td>4.1</td>
<td>4.2</td>
<td>2.9</td>
</tr>
<tr>
<td>11</td>
<td>7.9</td>
<td>1.7</td>
<td>155</td>
<td>172</td>
<td>4.2</td>
<td>6.3</td>
<td>25.5</td>
</tr>
<tr>
<td>12 S</td>
<td>6.6</td>
<td>2.1</td>
<td>184</td>
<td>174</td>
<td>2.0</td>
<td>6.5</td>
<td>14.0</td>
</tr>
<tr>
<td>13</td>
<td>6.9</td>
<td>1.9</td>
<td>183</td>
<td>194</td>
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REFERENCES