Factors Predictive of Ischemic Heart Disease Mortality in Foundry Workers Exposed to Carbon Monoxide

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The potential predictors of ischemic heart disease mortality were studied for 931 male foundry workers in Finland who participated in a health examination in 1973. These workers were followed up to 1993 through registers and by using a questionnaire. In 1973, the systolic and diastolic blood pressures of workers exposed to carbon monoxide (CO) were slightly higher than those of unexposed workers. The prevalence of angina pectoris showed a clear dose-response relation to CO exposure. Electrocardiogram (ECG) findings indicating past myocardial infarction or suggesting coronary artery disease as a function of smoking and/or CO exposure were not evident. In the 1987 follow-up, the rate ratio for ischemic heart disease mortality was estimated as 4.4 for CO-exposed smokers compared with unexposed nonsmokers. Ischemic heart disease mortality in 1973–1993 was analyzed by using the Cox proportional hazards model. The statistically significant predictors were age, pathologic ECG findings in 1973, regular CO exposure, and abundant alcohol drinking. Of the ECG findings, changes in Q or QS and ST-J or ST waves and in ventricular extrasystoles were statistically significant. The risk of mortality from ischemic heart disease was increased by working in iron foundries, by hypertension, and by smoking. Am J Epidemiol 2000;152:628–32.

The best-known risk factors for cardiovascular diseases are of nonoccupational origin: high blood pressure, high levels of low density lipoprotein cholesterol and low levels of high density lipoprotein cholesterol, and smoking. However, even occupational and environmental factors, such as shift work (1), job strain (2), physical inactivity at work (3), unemployment (4), passive smoking (5), and exposure to carbon monoxide (CO) (6), have been of concern. For instance, exposure to CO at levels at or above current New York City standards has been associated with a significant 35 percent increase in ischemic heart disease mortality (7). In addition, during long-term follow-up, the interaction of different risk factors will confound the association between CO exposure and cardiovascular disease.

In 1973, the Finnish Institute of Occupational Health (Helsinki, Finland) carried out a health examination of 931 current foundry workers. Included were measurements of systolic and diastolic blood pressure and of body mass index, an electrocardiogram (ECG), and a questionnaire on angina pectoris (8). The results showed that the systolic and diastolic blood pressures of CO-exposed workers were slightly higher than those of unexposed workers when age and smoking habits were taken into consideration (9). The prevalence of angina pectoris showed a clear dose-response relation to CO exposure for occupation, smoking, or both. Not evident were ECG findings of past myocardial infarction or coronary artery disease as a function of smoking, CO exposure, or both.

Follow-up of the same cohort in 1987 showed that the age-standardized incidence densities per 1,000 persons for compensated medication for hypertension were 9.1 for unexposed nonsmokers and 21.4 for exposed smokers (rate ratio (RR) = 2.3, 95 percent confidence interval (CI): 0.97, 6.35). The difference in the entire cohort was caused by the greatest difference among iron foundry workers, for whom the rates were 8.1 and 24.0, respectively (RR = 3.0, 95 percent CI: 0.96, 9.78) (10). The age-standardized mortality rates for ischemic heart disease were 1.0 for nonsmokers with no or slight occupational CO exposure and 7.3 for exposed smokers (95 percent CI: 1.39, 60.96). The Poisson multiplicative regression model estimated the rate ratio as 4.4 (95 percent CI: 1.27, 15.08) for CO-exposed smokers compared with unexposed nonsmokers.

The aim of the present study was to estimate the potential predictive value of the 1973 cardiovascular health examination for ischemic heart disease mortality in foundry workers during 20 years of prospective follow-up.

MATERIALS AND METHODS

Subjects

This study comprised 931 men hired in 1950–1972 by 20 foundries. The men were still actively working in foundries...
in 1972, had been potentially exposed to CO for at least 4.2 years, and took part in a health examination in 1973. They completed a questionnaire on symptoms and diagnosed diseases, including a history of chest pain and cardiovascular diseases diagnosed by a physician, as well as smoking habits. Blood pressure and body mass index measurements were included in the health examination, as was a 12-lead resting ECG (9). The data collection methods have been described in detail previously (9, 11). The study was based on an agreement with labor market organizations, and the Research Committee of the Finnish Institute of Occupational Health approved the research protocol. Participation in the study was voluntary and was based on written information. The ECGs were coded according to the Minnesota code (8); ventricular extrasystoles were coded by using the Scandinavian ECG classification (12). ECG findings were also classified as indicative of past myocardial infarction (Minnesota codes 1.1, 1.2 + 5.1, or 1.2 + 5.2) or suggestive of coronary disease (any of codes 1.2–1.3, 4.1–4.3, 5.1–5.2, 6.1–6.2, 7.1–7.2, or 7.4 or 8.3) (9, 13).

The same foundry workers were followed up to 1993 through registers and by using a questionnaire. The vital statuses and addresses of the workers were traced through the Population Information System. Causes of death categorized according to the International Classification of Diseases, Eighth Revision (14) were acquired from Statistics Finland, and codes 410.00–414.99 were classified as ischemic heart disease. Morbidity from cardiovascular diseases during follow-up was measured with the use of medication, for which special compensation (80–100 percent) is granted by the national sickness insurance law. Coronary heart disease, cardiac insufficiency, cardiac arrhythmia, and hypertension were the cardiovascular diseases for which specially compensated medicines could be granted. Data on specially compensated medication were obtained from the Social Insurance Institution. The questionnaire study on occupational history, smoking, and drinking habits was carried out in 1993.

Exposures

In 1972, CO levels were measured in 52 iron, 10 steel, and 5 nonferrous foundries (15). The hygienic standard for CO (50 cm$^3 \times m^3$) was exceeded in 72 percent of the air samples from the iron foundries, 9 percent of the samples from the steel foundries, and 20 percent of the samples from the nonferrous foundries. The blood carboxyhemoglobin content of iron foundry workers exceeded 6 percent in 71 percent of the smokers and 28 percent of the nonsmokers. On the basis of these CO measurements, the foundry occupations were divided into three categories: 1) regular CO exposure: casters, furnacemen, and knockout men; 2) occasional or slight CO exposure: fellters, truck drivers, crane operators, and loader drivers; and 3) no CO exposure: floor molders, machine molders, coremakers, ingot casters, and other workers. To analyze the data, the lifetime time-weighted average of the three CO exposure scores obtained until the end of 1992 from the questionnaire was used to define the main exposure category for each worker.

Potential confounding exposure to polycyclic aromatic hydrocarbons and heat was controlled for in the follow-up until 1987 (10). No dose-response relation was found between this exposure and cardiovascular diseases. Confounding exposure to heat was difficult to control, because the same occupational groups were exposed to both CO and heat. At the time of the health examination (1972–1973), there were no remarkable differences in the degree of heat present in the iron and steel foundries; however, differences in CO exposure were evident (15). In the 1987 follow-up, the dose response according to CO exposure and smoking was more evident for iron foundry workers than for steel and nonferrous foundry workers (the total number of nonferrous foundry workers was very small, only 53) (10).

The confounding effect of smoking was controlled for in the analysis. Smoking habits were classified according to the questionnaire data received in 1993. These data showed good validity when compared with those obtained in 1973 (93 percent of the respondents were in the same smoking category 20 years later) (10).

Similarly, the confounding effect of alcohol drinking was controlled for in the analysis on the basis of the 1993 questionnaire data. The questionnaire classified lifetime alcohol drinking into three categories: abundant, moderate, or no use.

Statistical analysis

Ischemic heart disease mortality in 1973–1993 was analyzed with the Cox proportional hazards model (16, 17). Parameters of the model were estimated by using the partial likelihood method. Interaction tests were based on the likelihood ratio test (used when there are two or more parameters) or the Wald chi-square test for the parameter (used when interaction comprises only a single parameter). Interactions between the following variables were tested: smoking and CO exposure, ECG and angina pectoris, type of foundry (iron, steel, or nonferrous) and CO exposure, and hypertension and angina pectoris. The SAS software system (version 6.12; SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis.

The following variables measured during the 1973 health examination were incorporated into the model: age, body mass index, hypertension and angina pectoris. The SAS software system (version 6.12; SAS Institute, Inc., Cary, North Carolina) was used for statistical analysis.

The following variables measured during the 1973 health examination were incorporated into the model: age, body mass index, hypertension (yes, if diastolic blood pressure was ≥295 mmHg or systolic blood pressure was ≥160 mmHg; no, if diastolic blood pressure was <95 mmHg and systolic blood pressure was <160 mmHg), mild or severe angina pectoris (whether prevalent or not; classified according to Rose and Blackburn (8)), and ECG findings (pathologic, slight changes, or normal) (9). The following variables were obtained by questionnaire in 1993: duration of foundry employment, main type of foundry (iron, steel, or nonferrous), category of CO exposure (regular, occasional, or no), smoking habits classified according to lifelong smoking history (current smokers, former smokers, or nonsmokers), and alcohol drinking habits (abundant, moderate, or no use). In addition, separate models were computed for different ECG patterns (if changes were abnormal or not) as well as for the
combined variables indicative of past myocardial infarction and suggestive of coronary heart disease classified according to Pyörälä et al. (13). Persons who had reported on the 1973 questionnaire earlier diagnosed heart disease or diagnosed hypertension or who had a registered specially compensated medication for these diseases were excluded from the model (a total of 65 men).

RESULTS

In the model, the statistically significant predictors of ischemic heart disease death were age, pathologic ECG findings, regular CO exposure, and abundant alcohol drinking (table 1). The risk of mortality from ischemic heart disease was increased by working in iron foundries, by hypertension, and by smoking, but the effect of these factors did not reach a statistical significance of \( p = 0.05 \). The rate ratio for current smoking was regularly about 2.00 in the models, but when the abundant alcohol drinking variable was included, the standard error of the coefficient of the smoking variable increased. Therefore, the rate ratio for current smoking was not statistically significant. The rate ratio for CO exposure decreased slightly when only age and smoking were controlled for (regular exposure: \( RR = 1.97 \), 95 percent CI: 0.94, 4.16; occasional exposure: \( RR = 1.72 \), 95 percent CI: 0.87, 3.38) (data not shown). The other variables, body mass index and number of years of exposure, did not explain the findings for ischemic heart disease mortality.

A pathologic ECG finding in 1973 was an important predictor of ischemic heart disease mortality. Current smoking or abundant alcohol drinking did not decrease its significance as a predictor. When this variable was excluded from the model, the coefficients of the other variables essentially did not change.

In detailed analysis by type of ECG abnormality (table 2), changes in Q and QS waves and ST-J and ST waves and in uni- or multifocal ventricular extrasystoles were statistically significant. The rate ratio for the combined indicative myocardial infarction variable was statistically significant at 2.26. The other combined variable, suggestive coronary heart disease, that is, ECG changes suggestive of coronary artery disease, had a rate ratio of 1.64 that did not reach statistical significance, however.

In the model in which the indicative myocardial infarction variable was used instead of the unspecified pathologic ECG finding variable, hypertension also was a statistically significant predictor of mortality from ischemic heart disease. When the variable defined as compensated medication for congestive heart failure (including medication for coronary heart disease, cardiac insufficiency, or cardiac arrhythmia) was added to the model, its role as a predictor was negligible. The same was true for the variables defined as compensated medication for hypertension and as years of medication for hypertension. The coefficient of the years of medication for hypertension variable was negative but not statistically significant. Thus, medication for hypertension decreased ischemic heart disease mortality slightly.

**DISCUSSION**

The causal effect of long-term occupational CO exposure on cardiovascular diseases is difficult to evaluate because the biologic mechanism is complex (6, 18). Furthermore, there are only a few high-quality methodological epidemiologic studies on this topic (6). Occupational exposure to CO is often confounded or modified by individual habits or characteristics or by other occupational exposures (3, 6, 19). All of them cannot be similarly controlled for in each study; for example, diet habits, cholesterol, and physical activity were not measured in the present study. In addition, foundry workers are selected into and out of jobs for health reasons, and health selection also hampers interpretation of the results (20).

The Finnish workers in the steel and nonferrous foundries were exposed to less CO than those in the iron foundries. The carboxyhemoglobin levels of iron foundry workers were high. Furthermore, the carboxyhemoglobin levels of smokers were clearly higher than those of nonsmokers. Therefore, the effect of occupational CO exposure was obviously increased by smoking (15).

In the 1973 Finnish cross-sectional study, high prevalences of symptoms suggestive of ischemic disease (14 percent) and of ECG changes suggestive of coronary heart disease (15 percent) were observed for foundry workers (9). However, the ECG changes did not follow any consistent

### TABLE 1. Variables associated with the risk of mortality from ischemic heart disease among Finnish foundry workers during the follow-up period 1973–1993

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rate ratio*</th>
<th>95% confidence interval</th>
<th>( p ) value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1973)</td>
<td>1.10</td>
<td>1.06, 1.13</td>
<td>0.00</td>
</tr>
<tr>
<td>Body mass index (1973)</td>
<td>1.00</td>
<td>0.91, 1.11</td>
<td>0.94</td>
</tr>
<tr>
<td>Hypertension (1973)</td>
<td>1.51</td>
<td>0.85, 2.66</td>
<td>0.16</td>
</tr>
<tr>
<td>Angina pectoris (1973)</td>
<td>1.10</td>
<td>0.90, 1.34</td>
<td>0.35</td>
</tr>
<tr>
<td>Pathologic ECG‡ (1973)</td>
<td>1.60</td>
<td>1.13, 2.26</td>
<td>0.01</td>
</tr>
<tr>
<td>No. of exposure years</td>
<td>0.99</td>
<td>0.96, 1.02</td>
<td>0.53</td>
</tr>
<tr>
<td>Iron foundry</td>
<td>1.88</td>
<td>0.44, 7.93</td>
<td>0.39</td>
</tr>
<tr>
<td>Steel foundry</td>
<td>1.12</td>
<td>0.25, 5.06</td>
<td>0.88</td>
</tr>
<tr>
<td>Regular carbon monoxide exposure</td>
<td>2.15</td>
<td>1.00, 4.63</td>
<td>0.05</td>
</tr>
<tr>
<td>Occasional carbon monoxide exposure</td>
<td>1.80</td>
<td>0.91, 3.57</td>
<td>0.09</td>
</tr>
<tr>
<td>Current smoker</td>
<td>1.87</td>
<td>0.78, 4.46</td>
<td>0.16</td>
</tr>
<tr>
<td>Former smoker</td>
<td>1.05</td>
<td>0.41, 2.69</td>
<td>0.92</td>
</tr>
<tr>
<td>Abundant alcohol drinker</td>
<td>4.16</td>
<td>1.44, 12.00</td>
<td>0.01</td>
</tr>
<tr>
<td>Moderate alcohol drinker</td>
<td>1.23</td>
<td>0.67, 2.25</td>
<td>0.50</td>
</tr>
</tbody>
</table>

* In the Cox proportional hazards model, rate ratio is equal to the exponent function of the corresponding coefficient.
† The significance of the test that the rate ratio is 1.00.
‡ ECG, electrocardiogram.
TABLE 2. Risk of mortality from ischemic heart disease, by type of electrocardiogram (ECG) abnormality, of Finnish foundry workers during the follow-up period 1973–1993†

<table>
<thead>
<tr>
<th>Type of ECG abnormality‡</th>
<th>Rate ratio§</th>
<th>p value§</th>
<th>Age (1973)</th>
<th>Body mass index (1973)</th>
<th>Hypertension (1973)</th>
<th>Angina pectoris (1973)</th>
<th>No. of exposure years</th>
<th>Foundry</th>
<th>Carbon monoxide exposure</th>
<th>Smoker</th>
<th>Alcohol drinker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q, QS</td>
<td>4.21</td>
<td>0.00</td>
<td>1.09*</td>
<td>0.99</td>
<td>1.74</td>
<td>1.12</td>
<td>0.99</td>
<td>1.70</td>
<td>1.01</td>
<td>1.96</td>
<td>1.65</td>
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<tr>
<td>QRS</td>
<td>0.41</td>
<td>0.40</td>
<td>1.10*</td>
<td>0.99</td>
<td>1.67</td>
<td>1.09</td>
<td>0.99</td>
<td>1.70</td>
<td>1.11</td>
<td>1.96</td>
<td>1.84</td>
</tr>
<tr>
<td>R</td>
<td>2.07</td>
<td>0.07</td>
<td>1.10*</td>
<td>1.00</td>
<td>1.53</td>
<td>1.11</td>
<td>0.99</td>
<td>1.71</td>
<td>1.06</td>
<td>1.93</td>
<td>1.79</td>
</tr>
<tr>
<td>STJ, ST</td>
<td>2.98</td>
<td>0.08</td>
<td>1.10*</td>
<td>1.00</td>
<td>1.43</td>
<td>1.08</td>
<td>0.96</td>
<td>1.67</td>
<td>0.96</td>
<td>2.31</td>
<td>1.90</td>
</tr>
<tr>
<td>T</td>
<td>2.10</td>
<td>0.06</td>
<td>1.10*</td>
<td>1.01</td>
<td>1.54</td>
<td>1.11</td>
<td>0.99</td>
<td>1.66</td>
<td>1.01</td>
<td>2.00</td>
<td>1.78</td>
</tr>
<tr>
<td>Atrial-ventricular conduction defect</td>
<td>3.79</td>
<td>0.08</td>
<td>1.09*</td>
<td>0.99</td>
<td>1.67</td>
<td>1.09</td>
<td>0.99</td>
<td>1.67</td>
<td>1.11</td>
<td>2.08</td>
<td>1.84</td>
</tr>
<tr>
<td>Ventricular conduction defect</td>
<td>1.58</td>
<td>0.40</td>
<td>1.10*</td>
<td>1.00</td>
<td>1.68</td>
<td>1.10</td>
<td>0.99</td>
<td>1.69</td>
<td>1.09</td>
<td>1.70</td>
<td>1.09</td>
</tr>
<tr>
<td>All arrhythmias</td>
<td>1.70</td>
<td>0.20</td>
<td>1.10*</td>
<td>1.00</td>
<td>1.60</td>
<td>1.10</td>
<td>0.99</td>
<td>1.63</td>
<td>1.04</td>
<td>2.13</td>
<td>1.86</td>
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<tr>
<td>Ventricular extrasystoles</td>
<td>3.55</td>
<td>0.05</td>
<td>1.10*</td>
<td>0.99</td>
<td>1.59</td>
<td>1.08</td>
<td>0.99</td>
<td>1.67</td>
<td>1.08</td>
<td>2.17</td>
<td>1.87</td>
</tr>
<tr>
<td>“Miscellaneous items at rest”</td>
<td>1.75</td>
<td>0.08</td>
<td>1.10*</td>
<td>0.99</td>
<td>1.61</td>
<td>1.10</td>
<td>0.99</td>
<td>1.78</td>
<td>1.10</td>
<td>2.08</td>
<td>1.83</td>
</tr>
<tr>
<td>Indicative myocardial infarction</td>
<td>2.26</td>
<td>0.03</td>
<td>1.10*</td>
<td>1.00</td>
<td>1.79</td>
<td>1.10</td>
<td>1.00</td>
<td>1.59</td>
<td>0.98</td>
<td>1.87</td>
<td>1.84</td>
</tr>
<tr>
<td>Suggestive coronary heart disease</td>
<td>1.64</td>
<td>0.09</td>
<td>1.10*</td>
<td>0.99</td>
<td>1.58</td>
<td>1.11</td>
<td>1.00</td>
<td>1.71</td>
<td>1.09</td>
<td>2.00</td>
<td>1.89</td>
</tr>
</tbody>
</table>

* Significance of the coefficient, p < 0.05.
† The Cox proportional hazards model was used; pathologic ECG as explanatory variable (table 1) was analyzed separately according to type of ECG abnormality.
‡ Q, QS: Minnesota code (MC) (8) 1.1–1.2; QRS: MC 2.1–2.5; R: MC 3.1–3.3; STJ, ST: MC 4.1–4.4; T: MC 5.1–5.4; atrial-ventricular conduction defect: MC 6.1–6.3; ventricular conduction defect: MC 7.1–7.6; all arrhythmias: MC 8.0–8.9; ventricular extrasystoles: Scandinavian code (12) VIII 1.1–5; ‘miscellaneous items at rest’: MC 9.0–9.8; indicative myocardial infarction: MC 1.1, 1.2 + 5.1, or 1.2 + 5.2; suggestive coronary heart disease: MC any of 1.2–1.3, 4.1–4.3, 5.1–5.2, 6.1–6.2, 7.1–7.2, or 7.4 or 8.3.
§ Refers to the corresponding ECG abnormality type variable after control for the other variables in the row.
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REFERENCES