Coffee and Alcohol Consumption as Triggering Factors for Sudden Cardiac Death: Case-crossover Study

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Aim. To estimate the relative risk of triggering sudden cardiac death after coffee or alcohol consumption in out-of-hospital sudden cardiac death victims.

Methods. A case-crossover design with usual frequency approach was used and the study population included persons who died out of hospital due to sudden cardiac death. By mailing 2 questionnaires, 1 to the family members of the deceased and the other to the attending physician, necessary data on the mode of cardiac death, life style, health, and several socio-demographic variables were obtained. Cases were those who died of sudden cardiac death within 1 hour after coffee consumption or within 2 hours after ingesting alcohol; but controls were those who died in the hours when they were not exposed to these stimulants. The relative risk of dying within exposed hours in comparison to non-exposed hours was parameter estimated for each risk factor.

Results. Among 309 sudden cardiac death victims who died in the period from January 2000 to March 2001 in Slovenia, there were 253 men and 56 women with median age at death of 57.1 and 57.7, respectively. On average, each of them had 2.8 risk factors for ischemic heart disease, and the estimated relative risk of dying during 1 hour after coffee consumption was 1.73 (95% confidence interval [CI] = 1.13-2.65), and within 2 hours after alcohol consumption 3.00 (95% CI = 1.61-5.68). Within both coffee drinking and alcohol consuming groups, the relative risk was different among persons with different life style habits. It ranged from 1.50 for the coffee drinkers who had been receiving medication due to risk factors of heart diseases, to 2.63 for former alcohol drinkers. Among alcohol consumers it varied from 2.66 among those who were performing less than 104 hours of physical activity of six metabolic equivalents at least, to 52.15 among those of 90 heart beats or more per minute.

Conclusion. Our research confirmed the hypothesis that coffee or alcohol consumption is a potential trigger for sudden cardiac death in persons with risk factors for ischemic heart disease.

Key words: adult; alcoholic beverages; coffee; cross-over studies; death, sudden, cardiac

Diseases of the circulatory system are the most frequent cause of death in the Western countries (1), and sudden cardiac death is a significant public health problem. Approximately 1 out of 1,000 persons dies per year due to sudden death, and 88% of these deaths are of cardiac origin (2).

Many of the risk factors associated with sudden cardiac death are the same as those with coronary artery disease (3), but the exact mechanism and interactions among them are not well understood (4). Also, the role of events triggering sudden cardiac death is not sufficiently explained.

Coffee drinking and alcohol consumption accelerate sympathatetic nerve activity (5-8). Higher risk for coronary syndrome exists for those who consume 5 or more cups of coffee per day than among those who do not drink coffee at all (9,10). Other reports say that caffeine cannot increase the risk of coronary or cerebrovascular diseases (11,12).

More than 5 drinks of alcoholic beverages a day were connected with the increased risk of sudden cardiac death. The highest incidence was found among heavy drinkers. Sudden cardiac death in connection with alcohol drinking was recognized as risky in persons with pre-existing ischemic heart disease (8,13).

According to our knowledge, the influence of coffee drinking and alcohol consumption on triggering sudden cardiac death has not been sufficiently explored, so we tried to specify the relative risk of triggering sudden cardiac death due to coffee drinking within 1 hour, and alcohol consumption within 2 hours after drinking each beverage. We also calculated the relative risk for groups of individuals with distinct life style, biological, or social risk factors.

Subjects and Methods

Population

The sample was selected on the basis of the underlying cause of death from the General Mortality Register of Slovenia.
The study comprised successive death of residents, aged from 20 to 65 years at the moment of death and died out of hospital due to cardiac disease from January 2000 until the end of March 2001.

Cases were sudden cardiac death victims who died during hours exposed to stimulants, meaning within 1 hour after drinking the last cup of coffee (50 ml), or within 2 hours after drinking the last international unit (IU) of alcohol. Controls were those who also died of a sudden cardiac death during unexposed hours (14). Risk hours were calculated by multiplying the cups of coffee consumed per day by 365 days of a year, and risk hours of alcohol consumption were obtained by multiplying the twofold number of IU of alcohol consumed on a typical drinking day by the number of such days in a year. Unexposed hours were obtained by calculating 8,760 hours minus exposed hours.

The mode of death, data on cardiac disease, and associated risk factors were obtained through 2 questionnaires. On the basis of the mode of death reported on the questionnaires and/or on a death certificate the deceased were divided into sudden cardiac death victims and expected deaths. Sudden cardiac death was defined as an instantaneous death or a death within 1 hour after the onset of cardiac symptoms. We analyzed only occasional or regular coffee drinkers, drinking up to 4.5 cups of coffee per day, and permanent or occasional alcohol consumers, consuming up to 5.5 international units (IU) of alcohol per drinking day. Chronic stress was defined as retirement or dismissal from employment in the last year of life or serious disease or death of a close family member in the same time period (15). Family history was positive, if some of the first-degree relatives, men before the age of 56, and women before 66, survived the attack of myocardial infarction or died due to it or to sudden cardiac death. Drugs currently used – the drugs which were prescribed in the period of at least 1 month before the person died. The additional information on drugs was reported by the family members when medical practitioner’s information was missing.

Smokers were regular, occasional, former, or never smokers. Physical activity was measured according to metabolic equivalents (MET), and hours per week (at least 2 hours per week – enough physically active). Systolic, diastolic blood pressure, heart frequency, ECG trace, blood cholesterol, and body mass index (BMI) were considered as binary variables also.

For calculating the average number of pathologic conditions per a deceased person, systolic and diastolic blood pressure, heart frequency, pathologic ECG trace, coronary artery disease in the deceased, life expectancy in life, cholesterol with fractions, triglycerides, diabetes, body mass index, and family history were taken into account.

Questionnaires

The first questionnaire was mailed to spouses or close relatives of the deceased and after receiving an answer from them the second questionnaire was sent to the attending physician. Questionnaires included data on life style, family history, eventual medication, stressful events in the last year of the deceased’s life, and some socioeconomic data. In addition, a very detailed description of the cups of coffee, and units of alcohol consumed by the deceased in the last 24 hours before death had to be put in a time line as well as the usual frequency of coffee and alcohol consumption per day and per year. Closed questions were used, with detailed instructions for completion. If the response was not received within 3 weeks, another request for participation was mailed to the same address. In case there was no answer to the second request, the case was considered to be non-responsive.

The questionnaire for the attending physician covered the data on the circulatory and biochemical parameters with some health issues.

The research protocol was approved by the Ethics Committee at the Ministry of Health of the Republic Slovenia, and all interviewed received a letter in which their rights concerning data protection and non-participation in the research were stated.

Statistical Analysis

We used a case-crossover study design, developed by Malcolm Maclure (14), an epidemiological method with the characteristics of a case control and cohort study at the same time. In this kind of a study the same subject crosses from a period or a state of a higher exposure to a risk factor to a lesser exposure or non exposed state when the risk factor is not acting any more. The method is suitable for assessing the influence of short time (minutes, hours, days) acting risk factors on the outcome of a specific event, like the influence of mobile telephones or benzodiazepines on traffic accidents, and sexual activity or alcohol consumption on myocardial infarction (15-17).

The short time acting risk factor was the elevated level of caffeine or alcohol in blood during a period of 1 hour or 2 hours after the consumption of a particular beverage whereas the specific outcome event was sudden cardiac death.

The observed parameter was the average incidence rate ratio – the relative risk (RR). It was estimated by dividing the number of discordant pairs of exposed cases (persons died within exposed hours) by the number of discordant pairs of unexposed controls (also died but in unexposed hours). The relative risk was calculated by dividing yearly unexposed hours of cases by yearly exposed hours of controls (14). An estimate of the natural logarithm of the standard error of the rate ratio was used for calculating 95% confidence interval suitable for cohort studies with a small number of cases (18).

For each dependent variable (coffee or alcohol consumption) the period of higher exposure was defined by minimal induction time and the highest frequencies of death on epidemiological histograms (Fig. 1).

SPSS statistical package for Windows (Version 10, SPSS Inc., Chicago, IL USA. License: Institute of Public Health of the Republic Slovenia) and Microsoft Excel statistical package for Windows (Version 5.1. 2600 Service Pack 1 Build 2600. Dell Computer Corporation. License: Institute of Public Health of the Republic Slovenia) were used for statistical analysis.

Results

Out of 600 questionnaires mailed to family members and attending physicians, from January 2000 till the end of March 2001, we received 374 responses, (62.3% response rate). The response rate of family members was 83.5% for coffee drinking and 53.9% for alcohol consumption. Three hundred and nine sudden cardiac death victims were identified according to the definition of sudden cardiac death, and were separated for a further analysis. The ratio between men and women was 5:1 in favor of women and median age at death was 57.1 years (range 50.4-62.1) for men and 57.7 years (range 48.3-60.9) for women. On average each decedent had 2.83 pathologic conditions connected with ischemic heart disease, and 26.2% of them had accompanying diseases.

Coffee Drinking

Out of 258 persons, 153 (59.3%), for whom we received the answers on coffee drinking, were regular coffee drinkers, 68 (26.4%) consumed coffee occasionally, and 37 (14.3%) did not drink coffee at all. Among regular and occasional drinkers 166 persons drank coffee on day when they died. We received 149 responses on the exact hour of the last coffee consumed and only these were used for the relative risk calculations.

The hazardous time of 1 hour was derived from the epidemiological histogram made on the population of 1 or fewer cups of coffee per day (Fig. 1). The relative risk of dying due to sudden cardiac death within an hour after drinking a cup of coffee was 73% higher (95% confidence interval [CI] 1.132-2.65) than in the hours when caffeine was not acting in the body.

Among the specific groups of coffee consumers, defined by a single risk factor, the relative risk for sudden cardiac death increased to a statistically significant level in men, regular tobacco smokers, and in...
persons who had been physically active more than 104 hours per year. In these persons, the relative risk increased with higher levels of physical activity from 6 to 7 MET. Decedents described as being under stress in the last year of their lives had the relative risk equal to about 2. The relative risk slightly increased also in persons with body mass index higher than 25, and among sudden cardiac death victims receiving medications. The relative risk approaching statistical significance was registered among regular and former drinkers, those with family history of sudden cardiac death or acute myocardial infarction, and persons who had an average systolic blood pressure 140 mm Hg or more (Table 1).

Alcohol Consumption

From 309 questionnaires we obtained 290 (93.9%) answers on alcohol consumption. Among them, there were 119 (41.0%) regular drinkers, 114 (39.3%) occasional drinkers, 37 (12.8%) former drinkers, and 20 (6.9%) persons who had never consumed alcohol. Of alcohol drinkers, 51.5% consumed less than 3 IU per drinking day, another 20% consumed up to 5.5 IU and the last quarter 6 or more IU of alcohol per drinking day. Out of 272 alcohol drinkers, 87 (32.0%) decedents consumed alcohol on the day they died and for 70 of them the hour of the last alcohol consumption was reported. The relative risk was calculated for those who had been drinking 5.5 IU per drinking day or less. Among them, minimal induction time for sudden cardiac death was half an hour, followed by an hour and a half for the highest incidence (Fig. 1B).

Among persons drinking alcohol, those who had on average 3.0 risk factors for ischemic heart disease had the relative risk within 2 hours after drinking alcohol of 3.00 (95%CI = 1.61-5.68). Among groups of alcohol consumers, defined by a single risk factor, relative risk was elevated in regular coffee drinkers, former smokers, those who had been performing physical activity of 6 or 7 MET, and in persons under chronic stress. Among circulatory parameters, heart frequency of 90 or more beats per minute, elevated systolic blood pressure and pathological ECG had elevated relative risk, and among biochemical measures, cholesterol level of more than 5 m mol/l appeared risky.

Persons receiving medication were also at increased relative risk (Table 2). For the majority of alcohol-consuming specific groups, the relative risk increase was from 6% to 86% above average.

Discussion

Our results are in accordance with the hypothesis that coffee or alcohol consumption could trigger sudden cardiac death. Drinking 1 to 5 cups of coffee per day significantly contributed to the risk of triggering sudden cardiac death during the first hour after coffee consumption and consuming up to 5.5 IU of alcohol per drinking day also elevated the relative risk for the first 2 hours.

Our results show that either coffee or alcohol consumption can trigger sudden cardiac death in persons under chronic stress, those who are overweight or obese, and those who were prescribed drugs for cardiac diseases. In addition, six or more MET of physical activity do not protect individuals with risk factors for ischemic heart disease when drinking coffee or alcohol. Coffee consumption can also trigger sudden cardiac death in regular smokers, and alcohol consumption can do the same in coffee drinkers and former smokers.

A case-crossover study design was developed as an answer to lowering the response rate in case control or cohort studies (14). At the same time it is the best method to avoid selection biases (16). Due to this, and because sudden cardiac death victims were assigned to cases and controls on the basis of the time lag between the last coffee or alcohol consumption and death, we thought that a 62.3% response rate was not a limitation for calculating the relative risk. With this kind of allocation, all the decedents had the same possibility to fall into either of the categories, which significantly decreased the selection bias.
The second obstacle that could influence the results were proxy respondents, an obligatory matter in mortality studies. Other studies suggest that members of the same household are good enough for proxy informants (19), as were the spouse or first degree relatives in our study.

The limitation was the small number of persons who drank coffee or alcohol on the day when they died and for whom we had to obtain the exact hour of the last consumption of a particular beverage. As a consequence of these preconditions, we ended with 21 cases in the coffee drinking group and 10 in the alcohol group. Due to this reduction in usable cases we could only count on the relative risk calculated for large subgroups with 7 to 10 cases, although the small number of cases is not a limitation for calculating the relative risk. Enlarging the total number of eligible cases and controls would lead to narrower confidence limits, establishing relations among subgroups, and possibility to adjust for confounding variables.

When we compare results of different studies on coffee consumption, it has to be remembered that different cultures make coffee on different ways, a cup of coffee does not mean the same amount of caffeine in all countries, not even for all individuals in the same country.

According to our knowledge, there are not many studies dealing with factors triggering sudden cardiac death, in contrast to myocardial infarction which is studied more frequently. In comparison with other studies, our results approached the findings of a meta-analysis of 8 case-control studies where the increased risk was found for drinking 5 cups of coffee per day versus non drinking (20), and Travois’s results published in 2001, on non fatal acute myocardial infarction odds ratio among non-smokers, and among current smokers drinking more than 3 cups of coffee per day, in comparison to non-smokers drinking 3 or less cups of coffee per day (21). Our results are also comparable with the relative risk described in Kagans study of sudden cardiac death among Hawaiian Japanese men (22). According to our research, coffee drinking can be a modifiable risk factor for sudden cardiac death in persons with positive family history because positive family history was found to be an independent risk factor for sudden cardiac death in middle aged men (4).

Data from more than 60 prospective studies have shown that people who drink small amounts of alcohol have lower rates of coronary heart disease than those who drink heavily or not at all (23-25). In our research, the range of relative risk for alcohol drinking is slightly higher than Laatikainen and his team published for alcohol related causes of death (26) or Bianchi for consuming more than 3 drinks per day (27), and is in accordance with Mc Elduff and

### Table 1. Relative risk of triggering sudden cardiac death within one hour after coffee consumption*

<table>
<thead>
<tr>
<th>Characteristic of the deceased*</th>
<th>No. of deceased</th>
<th>with information on the hour of the last coffee drinking</th>
<th>within one hour after coffee drinking</th>
<th>relative risk (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All deceased</td>
<td>149</td>
<td>21</td>
<td>1.73 (1.14-2.96)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>121</td>
<td>18</td>
<td>1.76 (1.11-2.79)</td>
<td></td>
</tr>
<tr>
<td>Regular drinkers</td>
<td>57</td>
<td>8</td>
<td>1.80 (0.90-3.60)</td>
<td></td>
</tr>
<tr>
<td>Former drinkers</td>
<td>19</td>
<td>4</td>
<td>2.63 (0.98-7.17)</td>
<td></td>
</tr>
<tr>
<td>Regular smokers</td>
<td>59</td>
<td>12</td>
<td>2.14 (1.21-3.77)</td>
<td></td>
</tr>
<tr>
<td>6 MET 104 or more hours a year</td>
<td>82</td>
<td>14</td>
<td>2.21 (1.31-3.73)</td>
<td></td>
</tr>
<tr>
<td>7 MET 104 or more hours a year</td>
<td>49</td>
<td>10</td>
<td>2.61 (1.41-4.85)</td>
<td></td>
</tr>
<tr>
<td>Stress described by family members</td>
<td>51</td>
<td>9</td>
<td>2.30 (1.19-4.42)</td>
<td></td>
</tr>
<tr>
<td>Family history about MI or SCD positive</td>
<td>36</td>
<td>6</td>
<td>2.09 (0.94-4.65)</td>
<td></td>
</tr>
<tr>
<td>BMI&gt;25kg/m²</td>
<td>115</td>
<td>17</td>
<td>1.84 (1.14-2.96)</td>
<td></td>
</tr>
<tr>
<td>Average systolic pressure 140 or more mm Hg</td>
<td>39</td>
<td>6</td>
<td>2.13 (0.96-4.74)</td>
<td></td>
</tr>
<tr>
<td>Receiving medication</td>
<td>109</td>
<td>15</td>
<td>1.75 (1.06-2.90)</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations: MET – metabolic equivalents; SCD – sudden cardiac death; BMI – body mass index.

### Table 2. Relative risk of triggering sudden cardiac death in 2 hours after alcohol consumption*

<table>
<thead>
<tr>
<th>Characteristic of the deceased*</th>
<th>No. of deceased</th>
<th>with an information on the hour of the last alcohol consumption</th>
<th>within 2 hours after alcohol consumption</th>
<th>relative risk (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>47</td>
<td>10</td>
<td>3.00 (1.61-5.68)</td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>44</td>
<td>10</td>
<td>3.03 (1.63-5.63)</td>
<td></td>
</tr>
<tr>
<td>Regular coffee drinkers</td>
<td>41</td>
<td>10</td>
<td>3.49 (1.88-6.49)</td>
<td></td>
</tr>
<tr>
<td>Former smokers</td>
<td>22</td>
<td>6</td>
<td>4.05 (1.82-9.01)</td>
<td></td>
</tr>
<tr>
<td>6 MET 1 to 104 hours a year</td>
<td>17</td>
<td>4</td>
<td>2.75 (1.03-7.33)</td>
<td></td>
</tr>
<tr>
<td>6 MET 104 or more hours a year</td>
<td>30</td>
<td>6</td>
<td>3.19 (1.42-7.10)</td>
<td></td>
</tr>
<tr>
<td>7 MET 1 to 104 hours a year</td>
<td>32</td>
<td>7</td>
<td>2.66 (1.27-5.58)</td>
<td></td>
</tr>
<tr>
<td>7 MET 104 or more hours a year</td>
<td>15</td>
<td>3</td>
<td>4.23 (1.36-8.13)</td>
<td></td>
</tr>
<tr>
<td>Chronic stress</td>
<td>16</td>
<td>4</td>
<td>4.05 (1.52-10.79)</td>
<td></td>
</tr>
<tr>
<td>Cholesterol &gt; 5 m mol/L</td>
<td>17</td>
<td>3</td>
<td>4.66 (1.50-14.45)</td>
<td></td>
</tr>
<tr>
<td>BMI&gt;25kg/m²</td>
<td>36</td>
<td>7</td>
<td>2.87 (1.37-6.02)</td>
<td></td>
</tr>
<tr>
<td>Heart frequency &gt;89 beats per minute</td>
<td>4</td>
<td>3</td>
<td>52.15 (16.82-161.70)</td>
<td></td>
</tr>
<tr>
<td>Average diastolic blood pressure &gt;90 mm Hg</td>
<td>11</td>
<td>3</td>
<td>5.60 (1.81-17.39)</td>
<td></td>
</tr>
<tr>
<td>Abnormal ECG</td>
<td>11</td>
<td>3</td>
<td>9.29 (3.00-28.80)</td>
<td></td>
</tr>
<tr>
<td>Receiving medication</td>
<td>31</td>
<td>7</td>
<td>3.07 (1.46-6.44)</td>
<td></td>
</tr>
</tbody>
</table>

*Abbreviations: MET – metabolic equivalents; SCD – sudden cardiac death; BMI – body mass index; ECG – electrocardiography.
Dobson’s results who published odds ratios for former moderate to heavy drinkers (28). As is known from the other studies (28,29) we also found that alcohol drinkers had the highest relative risk among alcohol consumers, and that the higher the grade of physical activity in trained or untrained persons was, the higher was the risk of dying. In both coffee and alcohol consuming groups, smoking and stress were found to significantly elevate the relative risk for triggering sudden cardiac death. In 2001 Marušić found synergistic interaction between smoking and neuroticism, a personality trait of emotional liability which has been to a certain extent related to individual differences in excitability and emotional responsiveness, which are reflected in increased reactivity to stressors (30).

To summarize, coffee drinking and alcohol consumption seem to be triggers for sudden cardiac death in persons with risk factors. Our results support the thesis that individuals who have risk factors for sudden cardiac death should be cautious in drinking alcohol or coffee especially in situations when more risk factors are at work at the same time. The relative risk, calculated for selected subgroups, characterized by particular variables, reflects the relative hazard that particular risk factor represents as a modifying factor. The importance of the research is in combining the impact of classical risk factors for sudden cardiac death with life style variables in assessing the relative risk of triggering sudden cardiac death. The research has to be continued because the calculation of relative risk would be more precise and confidence limits has to be continued because the calculation of relative risk of sudden coronary death. The research was funded by the Slovenian Ministry of Science and Research (Decision number OER-2199/SS, Code L3-1420-0312-99), and co-funded by the Ministry of Health and the Institute of Public Health of the Republic of Slovenia.

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