Alcohol and sudden cardiac death

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Abstract

Objective—To assess the relation between alcohol intake and sudden cardiac death—ie, death within one hour of the onset of symptoms.

Design—Prospective study of a cohort of men followed up for eight years.


Subjects—7735 men aged 40–59 at screening who were selected at random from one general practice in each of 24 towns.

Main outcome measure—All deaths from ischaemic heart disease with particular reference to those that were sudden (death within one hour of the onset of symptoms).

Results—During the follow up period of eight years there were 217 deaths from ischaemic heart disease of which 117 (54%) were classified as sudden. Although heavy drinkers (more than six drinks daily) did not show a high incidence rate of fatal heart attack, they showed the highest incidence rate of sudden cardiac death. This was seen in both manual and non-manual workers and most clearly seen in older (50–59) men. Death from ischaemic heart disease was more likely to be sudden in heavy drinkers than in other drinking groups; this phenomenon was seen irrespective of the presence or degree of pre-existing ischaemic heart disease. The positive association between heavy drinking and the incidence of sudden death was most apparent in men without pre-existing ischaemic heart disease, with heavy drinkers showing an increase of >60% compared with occasional or light drinkers. After adjustment for age, social class, and smoking, heavy drinkers free of pre-existing ischaemic heart disease had a marginally significantly higher incidence rates of sudden death than other drinkers combined (relative risk 2.00, 95% confidence interval 0.98 to 4.8). Additional adjustment for systolic blood pressure reduced the risk to 1.7.

Conclusions—This study suggests that heavy drinking is associated with an increased risk of sudden death. Studies that do not take pre-existing ischaemic heart disease into account are likely to underestimate the adverse effects of heavy drinking on the incidence of sudden death because the effects are not as evident in men with pre-existing ischaemic heart disease.

There is evidence that heavy drinking can induce cardiac arrhythmias and ventricular tachycardia, which are both mechanisms associated with sudden death. However, there is no consistent evidence from population studies that heavy drinking is associated with an increased risk of sudden death. Evidence for a strong association between alcohol and sudden death comes from studies on problem drinkers. Although several prospective studies have shown death in heavy drinkers to be predominantly sudden, the incidence of sudden death in these studies was not increased. Previous reports from the British Regional Heart Study have shown the prevalence of cardiovascular disease to be lowest in heavier drinkers possibly because of the tendency of men with ill health to drink less alcohol or abstain. Most of the population studies relating alcohol to sudden death have not taken pre-existing ischaemic heart disease fully into account. This paper examines the role of alcohol in sudden death, looking at the incidence of sudden death during the follow up after initial screening, as well as at the suddenness of death in men with and without pre-existing ischaemic heart disease, to assess whether alcohol intake contributes to either the rate at which sudden death occurs or to the proportion of deaths that are sudden.

Subjects and methods

The British Regional Heart Study is a prospective study of cardiovascular disease in 7735 men aged 40–59 years selected from the age-sex registers of one group general practice in each of 24 towns in England, Wales, and Scotland. The criteria for selecting the town, the general practice, and the subjects as well as the methods of data collection have been reported. Research nurses administered to each a standard questionnaire which included questions on smoking habits, alcohol intake, and medical history. Several physical measurements were made and blood samples (non-fasting) were taken for measurement of biochemical and haematological variables. The men were classified according to their current smoking status: those who had never smoked, ex-cigarette smokers, and current smokers. Those who had only ever smoked pipe/cigars were grouped as “never smoked”. Ex-cigarette
ALCOHOL INTAKE

Alcohol consumption was recorded on the basis of questions on frequency, quantity, and type that were similar to those used in the 1978 General Household Survey. The men were classified into five groups according to their weekly alcohol intake: none, occasional (<1 unit/week), light (1–15 units/week), moderate (16–42 units/week), and heavy (>42 units/week)—i.e., more than six drinks daily. One unit of alcohol is defined as half a pint of beer, a single measure of spirits, or a glass of wine (approximately 8–10 g alcohol). Non-drinkers included both life-long abstainers and ex-drinkers. Twenty five biochemical and haematological measurements on a single blood sample taken when the questionnaire was completed indicated that the reported levels of alcohol consumption were valid on a group basis.15

Pre-existing ischaemic heart disease

The men were asked to recall a doctor diagnosis of angina or myocardial infarction and several other disorders listed on the questionnaire. The World Health Organisation (WHO) (Rose) chest pain questionnaire was administered to all men at the initial examination17 and an electrocardiogram was recorded at rest from three orthogonal leads. The men were separated into three groups according to the evidence of ischaemic heart disease present at screening:

(I) No evidence of ischaemic heart disease on WHO chest pain questionnaire, electrocardiogram, or recall of a doctor diagnosis of ischaemic heart disease.

(II) Men with evidence suggesting ischaemic heart disease short of a definite myocardial infarction. This group contains those with electrocardiographic evidence of possible or definite myocardial ischaemia or possible myocardial infarction, those with angina or a possible myocardial infarction on WHO chest pain questionnaire, or with recall of a doctor diagnosis of angina.

(III) Men with a previous definite myocardial infarction on electrocardiogram or who recalled a doctor diagnosis of a heart attack. In the analyses men with pre-existing evidence of ischaemic heart disease consist of those in groups II and III.

FOLLOW UP

All men, whether or not they showed evidence of ischaemic heart disease at initial examination, were followed up for all cause mortality and cardiovascular morbidity.18 Information on death was collected through the established "tagging" procedures provided by the National Health Service registers in Southport (England and Wales) and Edinburgh (Scotland). Mortality and major ischaemic heart disease events (fatal and non-fatal) are based on eight years of follow up for each man. Fatal events were defined as death from ischaemic heart disease (ICD 9th revision codes 410–414) as the underlying cause. They comprised any death from ischaemic heart disease in an individual during the eight year follow up irrespective of a previous non-fatal event during that period. The certifying doctor was asked to complete an enquiry form which asked the duration from onset of symptoms to death: less than one hour, 1–24 hours, or greater than 24 hours. Sudden cardiac death was defined as an event in which death occurred within one hour of the onset of symptoms. Only those for whom clear information was available regarding death within one hour were included as sudden deaths. Suddenness of death is defined as the proportion of the deaths from ischaemic heart disease in any group that were manifest as sudden. A non-fatal myocardial infarction was diagnosed according to WHO criteria.19

STATISTICAL METHODS

Multiple logistic regression was used to obtain rates and relative risks adjusted for the various risk factors. Alcohol was fitted as four dummy variables for the five alcohol categories (non, occasional, light, moderate, and heavy) and in some of the analyses as one dummy variable—i.e., heavy versus the rest.

Results

During the follow up period of eight years there were 217 deaths from ischaemic heart disease of which 117 (53.9%) were classified as sudden, representing a crude attack rate for sudden cardiac death of 1.9/1000/year.

ALCOHOL AND SUDDEN DEATH FROM ISCHAEMIC HEART DISEASE

Figure 1 shows the crude attack rate/1000/year by alcohol intake for all deaths from ischaemic heart disease and for sudden and non-sudden deaths from ischaemic heart disease as well as the percentage of death manifest as sudden. Mortality from ischaemic heart disease decreased with increasing intake of alcohol intake up to levels of moderate drinking. Rates in heavy drinkers and light drinkers were similar. When deaths were separated into sud...
and sudden heart disease, there was a strong inverse association between alcohol intake and non-sudden death. For sudden death, however, there was no consistent pattern of relation except that heavy drinkers had the highest rates. Heavy drinkers had a significantly higher rate of sudden deaths than all other drinking groups combined (relative risk (RR) = 1.6, 95% confidence interval (CI) 1.0 to 2.6, \( p = 0.05 \)). Although heavy drinkers did not have an excess risk of overall death from ischaemic heart disease, death in heavy drinkers was more likely to be sudden than in any other drinking category. Seventy six percent of deaths from ischaemic heart disease in heavy drinkers occurred suddenly compared with 31% in non-drinkers. Among occasional, light, and moderate drinkers the proportion of suddenness of death was similar. Adjustment for age made little change to the overall relation between alcohol intake and risk of sudden death: heavy drinkers still showed the highest risk (fig 2). Indeed, since heavy drinkers tend to be younger, their relative risk increased with adjustment for age compared with all other drinking groups combined (RR = 1.8, 95% CI 1.1 to 2.9). Since alcohol has been shown in this study to be strongly associated with smoking and social class, further adjustments were made for social class and smoking. This also made little difference to the relation already observed (fig 2): heavy drinkers showed significantly higher risk than all other drinkers combined (RR = 1.73, 95% CI 1.06 to 2.86, \( p = 0.03 \)).

**ALCOHOL, AGE, AND SUDDEN DEATH**

We examined the relation between alcohol intake and sudden death in two age groups (table 1). Only in the older age group (50–59) was heavy drinking clearly associated with an increased risk of sudden death. In the younger age group occasional and heavy drinkers had similar rates, which were higher than those seen in other categories.

**ALCOHOL, SMOKING, AND SUDDEN DEATH**

Since alcohol intake is strongly associated with smoking status we have examined the relation between alcohol and sudden death according to smoking (data not presented). Only 14 of the 117 sudden deaths occurred in men who had never smoked so that no inference can be drawn about the alcohol-sudden death relation in this group of men. In ex-smokers (38 deaths), although the incidence of sudden death in heavy drinkers was not higher than in lighter drinkers, deaths in heavy drinkers were more likely to be sudden (75%) compared with the other drinking categories (50%). In current smokers (65 deaths), heavy drinkers had the highest absolute risk of sudden death, and death was also more likely to be sudden (75%).

**ALCOHOL, SOCIAL CLASS, AND SUDDEN DEATH**

We examined the relation between alcohol intake and sudden death separately in manual and non-manual workers. The incidence of sudden death was highest in heavy drinkers in both social classes even after adjusting for age and smoking but was most pronounced in manual workers. The adjusted relative risk of sudden death in heavy drinkers compared with all other drinking groups was 1.44 (99% CI 0.49 to 4.30) and 1.60 (95% CI 0.88 to 2.93) in non-manual and manual workers respectively. In both social classes deaths from ischaemic heart disease in heavy drinkers were also more likely to be sudden (100% in non-manual and 68% in manual workers).

**PRE-EXISTING ISCHAEMIC HEART DISEASE, ALCOHOL, AND SUDDEN DEATH**

We examined the relation between alcohol and sudden death separately in men with and without pre-existing ischaemic heart disease. Table 2 shows the crude mortality rates for all deaths from ischaemic heart disease and for sudden and non-sudden deaths from ischaemic heart disease according to the evidence of pre-existing ischaemic heart disease. Table 2 also shows age adjusted sudden death rates in the two groups.

**Men with no evidence of ischaemic heart disease**—No association was seen between alcohol intake and all deaths from ischaemic heart disease. Non-drinkers had the lowest rates of death from ischaemic heart disease. However, the risk of sudden death was significantly increased in heavy drinkers (\( p < 0.05 \)), who showed more than a twofold increase in risk compared with all other drinking groups after we adjusted for age (RR = 2.3, 95% CI 1.1 to 4.7). Indeed 82% of deaths occurring in heavy drinkers were manifest as sudden. There was a strong inverse relation between alcohol intake and non-sudden death.

**Men with pre-existing ischaemic heart disease**—In those with evidence of pre-existing ischaemic heart disease, non-drinkers showed the highest rate of deaths from ischaemic heart disease and moderate drinkers had the lowest rate. Heavy drinkers had rates lower than

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**Table 1** Alcohol intake and sudden death rates [1000] year by age

<table>
<thead>
<tr>
<th>Alcohol intake</th>
<th>40–49</th>
<th>No.</th>
<th>Rate</th>
<th>50–59</th>
<th>No.</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
<td>0</td>
<td>5</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occasional</td>
<td>11</td>
<td>1.5</td>
<td>22</td>
<td>2.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Light</td>
<td>8</td>
<td>0.9</td>
<td>31</td>
<td>2.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>1</td>
<td>0.1</td>
<td>20</td>
<td>2.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heavy</td>
<td>5</td>
<td>1.4</td>
<td>14</td>
<td>4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>25</td>
<td>92</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Figure 2. Alcohol intake and sudden death rates [1000]/year adjusted for age and in addition for social class and smoking.
occasional and light drinkers. The overall pattern was somewhat U-shaped. No association was seen between alcohol intake and the incidence of sudden deaths, but deaths from ischaemic heart disease in heavy drinkers were far more likely to be sudden (71% vs 38% in non-drinkers). A strong inverse association was seen for non-sudden death. Although the incidence of sudden death was significantly increased in men with pre-existing heart disease (4.6/1000/year vs 1.0-1.0/1000/year in men free of ischaemic heart disease), the proportion of death manifest as sudden was similar in both groups (50%-5% vs 56.3%).

ALCOHOL AND SUDDEN DEATH IN MEN WITH NO EVIDENCE OF ISCHAEMIC HEART DISEASE

Table 2 shows the relative risk of sudden death by the five alcohol categories adjusted for age and in addition for social class and smoking in men with no evidence of ischaemic heart disease. After adjustment for age, heavy drinkers had a significantly increased risk of sudden death compared with all drinking categories combined (p < 0.05). Although the numbers are small, after adjustment for age, social class, and cigarette smoking heavy drinkers had a twofold increase in risk of sudden death compared with all other drinkers combined. This difference was of marginal significance (p = 0.06). It is well established that heavy drinking raises blood pressure. To assess the effect of blood pressure on the relation between alcohol and sudden death we further adjusted for systolic blood pressure (table 3). This reduced the higher rates in heavy drinkers substantially. Compared with all the other drinking groups the risk was reduced from 2.03 to 1.73 and was no longer significant (p = 0.15). To assess whether the increased risk of sudden death in heavy drinkers could be attributed to antihypertensive treatment we examined the relations in table 3 after we excluded all men on regular antihypertensive treatment. Heavy drinking was still associated with a more than twofold increase in risk (RR = 2.25). Further adjustment for systolic blood pressure reduced the risk to 1.88, a similar level of risk seen when all men were included. This suggests that the increased incidence of sudden death in heavy drinkers is partly attributed to systolic blood pressure but not to antihypertensive therapy.

HEART RATE

Raised systolic blood pressure is associated with increased heart rate (r = 0.2, p < 0.0001). Adjustment for heart rate in addition to age, smoking, and social class resulted in a small reduction in relative risk (RR = 1.97). Additional adjustment for systolic blood pressure further decreased the relative risk to 1.67, indicating that heart rate alone was not responsible for the increased risk.

Discussion

In this study of middle aged British men we found a positive association between heavy drinking (>6 drinks daily) and the risk of sudden death: with heavy drinkers showing nearly a twofold increase in risk compared with other drinking categories combined. The increased incidence of sudden death in heavy drinkers was more pronounced in the older age group (50-59) and was seen in both social classes. The positive association was most clearly seen in those with no evidence of pre-existing ischaemic heart disease even after adjustment for age, social class, and smoking. Fatal heart attacks in heavy drinkers were predominantly sudden irrespective of age, social class, cigarette smoking, and presence of pre-existing ischaemic heart disease. Heavy drinking raises blood pressure, and about 10%

### Table 3 Alcohol intake and adjusted relative risk (95% CI) of sudden death in men with no evidence of IHD

<table>
<thead>
<tr>
<th>Age + smoking + social class</th>
<th>Age + smoking + social class + SBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>0</td>
</tr>
<tr>
<td>Occasional</td>
<td>1.00</td>
</tr>
<tr>
<td>Light</td>
<td>0.94 (0.40, 1.84)</td>
</tr>
<tr>
<td>Moderate</td>
<td>0.76 (0.32, 1.60)</td>
</tr>
<tr>
<td>Heavy</td>
<td>1.88 (0.78, 4.48)</td>
</tr>
<tr>
<td>Heavy vs rest</td>
<td>2.30 (1.11, 4.73)</td>
</tr>
</tbody>
</table>

SBP, systolic blood pressure.
of hypertension in middle-aged men may be attributed to heavy drinking.\textsuperscript{20} The increased incidence of sudden death in heavy drinkers in this study is partly attributed to the rise in systolic blood pressure associated with heavy drinking. After adjustment for systolic blood pressure there was still an increased incidence of sudden death (RR = 1.73) though the difference between heavy drinkers and other categories combined was not significant, possibly because of small numbers. These results and the finding that deaths from ischaemic heart disease in heavy drinkers are predominantly sudden suggest that alcohol may have a direct effect on initiating sudden cardiac death.

**PRE-EXISTING ISCHAEMIC HEART DISEASE**

About 50\% of those who die suddenly have symptoms or evidence of ischaemic heart disease before the event.\textsuperscript{21,22} People who develop ischaemic heart disease have an increased tendency to reduce or stop alcohol intake,\textsuperscript{13,14} so that studies that do not take pre-existing ischaemic heart disease into account are likely to underestimate the effects of heavy drinking on the incidence of sudden cardiac death. When we examined the relation between alcohol and incidence of ischaemic heart disease death in all men (including those with pre-existing ischaemic heart disease), heavy drinkers did not show excess risk of deaths from ischaemic heart disease but they showed the highest incidence rates of sudden cardiac death (fig 1). The increased risk was most apparent in men without evidence of ischaemic heart disease, with heavy drinkers showing a significantly increased risk of sudden death (table 2).

In those with pre-existing evidence of ischaemic heart disease, the incidence of sudden death was not increased in heavy drinkers. This group contains men with a wide range of severity and it is likely that even in this group those who remain heavy drinkers may have less severe ischaemic heart disease and thus be at lower risk of having a fatal attack. When we examined the relation separately in the small group of men with definite myocardial infarction (428 men), heavy drinking was associated with an increased but non-significant incidence of sudden cardiac death. However, in men both with and without pre-existing ischaemic heart disease the proportion of deaths that were sudden was highest in the heavy drinkers.

**RETROSPECTIVE STUDIES**

A study of 100 people who died suddenly and had a coroner’s necropsy in Newcastle-upon-Tyne showed a higher proportion of men had taken alcohol three hours before death than those who had a non-fatal myocardial infarction.\textsuperscript{23} Sudden death was defined as occurring less than 24 hours after onset of symptoms but 73\% took place within one hour. Interestingly, sudden death was most common on Saturdays, when drinking is most frequent and this was not seen for non-fatal myocardial infarction. Further, the sudden death group contained twice the proportion of men from social classes IV and V than the non-fatal myocardial infarction group (45\% vs 22\%). In the British Regional Heart Study we did not observe any difference in the occurrence of sudden death from ischaemic heart disease by day of the week but the effect of heavy drinking on the incidence of sudden death was more pronounced in manual workers than in non-manual workers. In the Auckland Study, which used community-based registers for myocardial infarction, heavy drinking discriminated between sudden (<24 hours) and non-sudden death.\textsuperscript{7}

**HEAVY DRINKING IN THE GENERAL POPULATION**

Although large population studies have shown problem drinking to be associated with a significant increase in risk of sudden death,\textsuperscript{4,10,11} the association between heavy drinking (variously defined) in the general population and sudden cardiac death has been inconsistent. Although most population studies have reported an inverse or U-shaped relation between alcohol intake and coronary heart disease mortality,\textsuperscript{12} studies which have examined the relation between alcohol intake and sudden cardiac death as a separate end point found a positive association or no association between heavy drinking (variously defined) and sudden death.\textsuperscript{24} Some of these studies, pre-existing ischaemic heart disease was not taken into account and in the ones that did so only men with definite ischaemic heart disease (variously defined) were excluded. In a prospective study of Finnish men aged 40–64 followed for five years, the sudden death rate increased with increasing alcohol intake and was more pronounced in the older men (over 50 years).\textsuperscript{9} This is consistent with the present study which found the incidence of sudden death to be much higher in heavy drinkers in the older age group (table 2). In the younger age groups (40–49 years) the incidence rate in heavy drinkers was similar to that in occasional drinkers. The increased rate of sudden death in younger occasional drinkers suggests that some of these may be binge drinkers, a condition that has been shown to be associated with cardiac arrhythmias which may lead to sudden death.\textsuperscript{2} In the Framingham study though the incidence of sudden death increased with age, deaths from ischaemic heart disease in younger men were more likely to be sudden.\textsuperscript{21} It is possible that occasional binge drinking in younger men may be responsible for this finding.

In a five year follow up of 269 755 American men aged 20–65 employed in the telephone industry, heavy drinking (>5 drinks a day) was associated with an increased risk of arrhythmic death but not with death in circulatory failure.\textsuperscript{25,26} However, in multivariate analysis, which included smoking and blood pressure among other variables, alcohol did not remain a significant predictor.\textsuperscript{26}

In the Framingham study, heavy drinking was apparently associated with unexpected sudden death—that is, sudden death in the absence of prior evidence of ischaemic heart disease.\textsuperscript{5} In both the Puerto Rican study\textsuperscript{14} and the Yugoslavian study\textsuperscript{15} no association was found between alcohol intake and the incidence of sudden death. However, in both these studies deaths from ischaemic heart disease in heavy drinkers were predominantly sudden (100\% and 85\% respectively). In the British Regional Heart Study the positive association
between heavy drinking and sudden death was less pronounced when pre-existing ischaemic heart disease was not taken into account. In the Puerto Rican study pre-existing ischaemic heart disease was not taken into account. In the Yugoslavian study only men with definite coronary heart disease were excluded. The positive association between heavy drinking and the incidence of sudden death is therefore likely to be underestimated in both these studies.

**NON-SUDDEN DEATH**

A strong inverse association that was apparent at levels of moderate drinking or above was observed with non-sudden death in this study even in men without pre-existing ischaemic heart disease. In men with pre-existing ischaemic heart disease the inverse relationship appeared to be continuous from non-drinkers through to heavy drinking. These findings suggest that alcohol may play a protective role in non-sudden fatal ischaemic heart disease but at levels of drinking which are associated with increased all-cause mortality and with several aspects of morbidity.27

**SUDDENNESS OF DEATH**

In most studies the conventional risk factors for ischaemic heart disease—smoking, blood cholesterol, and systolic blood pressure—have all been shown to be strongly predictive of the incidence of sudden death.22-31 However, these predictors have not been found to distinguish between the modes of death.22,23 The risk profile of an individual who dies suddenly cannot be distinguished from that of an individual who succumbs more slowly to ischaemic heart disease. However, findings from the British Regional Heart Study, the Auckland Study,7 the Puerto Rican study,8 and the Yugoslavian study9 indicate that death in an event of a heart attack in heavy drinkers was most likely to be sudden and that heavy drinking helps to discriminate between sudden death and non-sudden death.

In middle aged men in the British Regional Heart Study with no pre-existing ischaemic heart disease there was evidence that heavy drinking was associated with an increase in the incidence of sudden death as well as with the suddenness of death. Although the overall death rate from ischaemic heart disease was not high compared with lighter drinkers, the increased incidence rate of sudden deaths in heavy drinkers and the findings that deaths from ischaemic heart disease in heavy drinkers are predominantly sudden suggests that heavy drinking may precipitate arrhythmia and sudden cardiac arrest. The mechanism by which systolic blood pressure is increased with sudden cardiac death is uncertain. Several other studies also indicate that heavy drinking helps to discriminate between sudden death and non-sudden death. There is evidence from this study that heavy alcohol consumption may be a causative factor in sudden cardiac death. This has important implications in the aetiology and prevention of sudden death in all subjects but particularly those without pre-existing ischaemic heart disease.

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