Does binge drinking increase the risk of lung cancer: results from the Findrink study

Adetunji T. Toriola¹, Sudhir Kurl², Jari A. Laukkanen²,³, Jussi Kauhanen²,⁴

Background: There are controversies on the role of alcohol in lung cancer but no studies have examined the role of alcohol consumption patterns. We examined the association between binge drinking and lung cancer. Methods: Prospective population based study of 2267 middle aged men from Finland without a history of lung cancer at baseline. Results: There were 65 cases of lung cancer during an average follow-up of 16.7 years. The relative risk (RR) of lung cancer for binge drinkers was 1.89 (95% CI 1.10–3.20) after adjusting for age, examination year, family history of cancer, smoking, socio-economic status (SES), leisure-time physical activity and body mass index (BMI). No increased risk was observed among non-smoking binge drinkers, RR 1.48 (95% CI 0.89–2.47). Binge drinking smokers had increased risks of lung cancer in all categories of daily smoking compared with non-binge drinking smokers. The RR were 2.70 (95% CI 1.61–4.53), 2.35 (95% CI 1.38–3.96) and 2.24 (95% CI 1.29–3.80) for those who smoked 1–19, 20–29 and ≥30/day, respectively. Conclusion: Binge drinking is not associated with an increased risk of lung cancer among non-smokers but among smokers, it is associated with an increased risk irrespective of the number of cigarettes smoked daily. Even though the number of lung cancer cases among non-smokers was relatively small, the fact that the increased risk was limited to only smokers means that residual confounding by smoking may play a role. Larger studies are needed to clarify this association.

Keywords: alcohol, binge drinking, cohort study, drinking pattern, lung cancer.

Introduction

Studies examining the relationship between alcohol and lung cancer have often yielded conflicting results with some supporting a causal role for alcohol⁵ while others have reported no association.⁶–⁸ A pooled analysis of cohort studies reported a slightly greater risk of lung cancer only with alcohol consumption >30 g/day compared with no alcohol consumption.⁹ In a dose-specific meta-analysis and sensitivity analysis, evidence of an association between alcohol consumption and lung cancer was limited to groups consuming ≥2000 g of ethanol per month after adjusting for cigarette smoking.¹⁰ This may imply that the effects of alcohol on lung cancer are limited to heavier drinking.

There is no consensus on the definition of binge drinking. Binge drinking has been defined variously as the consumption of (i) five or more alcoholic beverages on one occasion,¹¹ (ii) six or more bottles of beer per drinking session,¹² (iii) eight drinks within the same day.¹³ Binge drinking pattern may have negative effects on health that can be disaggregated from usual drinking at various levels of consumption.¹⁴ The possibility of a relationship between lung cancer and binge drinking cannot be overlooked since binge drinking has been implicated with an increased risk of breast cancer¹⁵ but to date, no studies have been conducted on the risk of binge drinking and lung cancer.

Cigarette smoking is the most important risk factor for lung cancer, causing ~90% of cases,¹⁶ but it does not explain all the variations in the disease distribution.¹⁵ It has been suggested that alcohol consumption may explain some of the variations¹⁶ but the correlation of the two exposures usually complicates the analysis of their effects on lung cancer.¹

The tendency towards increased lung cancer rates among heavy alcohol consumers is the motive for this study and we hypothesize that binge drinking may be associated with an increased risk of lung cancer.

Methods

Study population

The present study is part of the Findrink study which was carried out among participants of a prospective cohort originally designed to investigate risk factors for cardiovascular diseases, and other health related outcomes in a population based sample of middle-aged men from Eastern Finland. Baseline examinations were conducted between March 1984 and December 1989. The study group is a representative sample of men living in Kuopio and its surrounding rural communities who were aged 42, 48, 54 and 60 years at the time of baseline examination. Of the 3235 eligible men, 2682 (83%) volunteered to participate and 198 were excluded because of death or serious disease. The baseline characteristics of the entire study population had been described previously.¹⁷ Of those, men who had a history of cancer at baseline were excluded from the present study series and complete data were available for 2267 men. The study protocol was approved by the Research Ethics Committee of the University of Kuopio and each participant gave written informed consent.

Alcohol consumption

Alcohol consumption was assessed with a structured quantity and frequency method using the Nordic alcohol consumption inventory.¹⁸,¹⁹ Usual frequency of intake and usual dose (in glasses or bottles) were recorded for each type of drink (beer, wine, strong wine, spirits) with a structured response form which assessed both total alcohol intake and the timing or pattern of drinking (usual number of drinks per session).
The measures of average weekly intake of all alcoholic beverages were calculated on the basis of known alcohol content of each type of drink and reported doses and frequencies of drinking sessions. A third of a litre bottle of ordinary beer (Class iii in Finland) contains 12 g of ethanol, strong beer (Class iv) contains 14 g of ethanol which is the ethanol equivalent of one portion of hard liquor. In this cohort, binge drinking was classified as the consumption of more than 70 g of ethanol at one drinking session. This is equivalent to the consumption of (i) six or more bottles of beer; (ii) one or more big bottle (75 cl) of mild wine; (iii) three-fourth or more of one big bottle (75 cl) of strong wine and (iv) ≥5 portions of hard liquor. Serum gamma-glutamyl transpeptidase (GGT) and mean corpuscular volume (MCV) were determined from baseline blood samples as biomarkers of excessive alcohol use. There was a correlation between serum GGT and alcohol consumption.

Ascertainment of lung cancer

Incident cases were derived from the population based Finnish Cancer Registry. All cancer cases diagnosed in Finland since 1953 are reported to the Finnish Cancer Registry and coverage of the national cancer registry is virtually complete with no loss to follow-up. Our study cohort was record linked with the cancer registry data by using the personal identification code. Every resident of Finland has a unique personal identifier that is used in registries. All lung cancer diagnoses that occurred between the study entry (March 1984 to December 1989) and December 2005 were included.

Smoking

In the exposure questionnaire, subjects were asked if they were smokers or not. Smokers were asked if they smoke regularly and how old they were when they started smoking regularly. A subject was described as a smoker if he had ever smoked on a regular basis and had smoked cigarettes, cigars or pipe within the past 30 days. Among smokers, the number of cigarettes, cigars and pipefuls of tobacco currently smoked daily and the duration of regular smoking in years were recorded on a self-administered questionnaire that was checked by an interviewer. The life-long exposure to smoking is the number of cigarettes an individual smokes daily multiplied by the number of years the individual has been smoking. We categorized the cohort into four based on both daily smoking habits and three based on duration of smoking in years. For daily smoking, the four categories are (i) non-smokers; (ii) those who smoke between 1 and 19 cigarettes daily; (iii) those who smoke between 20 and 29 cigarettes daily and (iv) those who smoke ≥30 cigarettes daily. For duration of smoking, the three categories are (i) non-smokers; (ii) those who have smoked for <30 years and (iii) those who have smoked for ≥30 years.

Other variables

Height and weight were measured at the time of baseline examination. Leisure time physical activity was assessed from a 12-month history, modified from the Minnesota Leisure time physical activity questionnaire. For each activity performed, the subjects were asked to record the frequency (number of sessions per month), average duration (hours and minutes per session) and intensity which were expressed in metabolic equivalents (METS). Food consumption was assessed at the time of blood sampling during the baseline phase of the study. Subjects were instructed on the use of household measures for quantitative recording of their food intake during the 4 days of data collection. A nutritionist gave the instructions and checked the completed food intake records. Dietary intake of foods and nutrients was calculated using NUTRICA software (version 2.5; National Public Health Institute, Turku). The software is compiled using mainly Finnish values of nutrient composition of foods, and takes into account losses of vitamins in food preparation. The nutrient composition of foods in the NUTRICA software used reflects data on vitamin contents of fruits and vegetables.

Socio-economic status (SES) was measured as a summary index that combined measures of income, education, occupation, occupational prestige, material standard of living and housing conditions. A high value on the SES index indicated a low socio-economic state.

Statistical analysis

Descriptive data are presented as means and SD for continuous data and percentages for categorical data. The relationship between binge drinking and risk of lung cancer was examined using the Cox proportional Hazards model. The following covariates were used: smoking history (daily smoking and duration of smoking in years), age, examination year, family history of cancer, SES, leisure-time physical activity and body mass index (BMI). Analyses were carried out in the whole cohort and among smokers alone. Analyses were also carried out in categories using the number of cigarettes smoked daily and duration of smoking, in years. Co-variates were selected on the basis of their previous roles as predictive factors on outcome event from previous evidence and available data. SPSS software version 15 was used for statistical analysis. Test for statistical significance were two-sided and differences with \( P < 0.05 \) were considered statistically significant.

Results

In the study cohort, 621 men (27% of study population) engaged in binge drinking while 1646 did not. There were 65 incident cases of lung cancer during the average follow-up time of 16.7 years. There were 27 cases of lung cancer among binge drinkers compared with 38 among non-binge drinkers. There was no significant difference in the mean age of binge drinkers (52.4 years) and non-binge drinkers (53.1 years) and their vegetable consumption. Binge drinkers had significantly higher mean BMI, lower mean SES index, smoked more cigarettes and consumed less fruits and berries. Their weekly mean alcohol consumption was significantly higher (192.2 vs. 48.9 g/week) than non-binge drinkers. Biochemical markers of excessive alcohol use such as serum GGT and MCV were also significantly higher among binge drinkers compared with non-binge drinkers (table 1).

Relative risk (RR) of lung cancer among binge drinkers in the whole cohort was 1.89 (95% CI 1.10–3.20) after adjusting for age, smoking, examination year, family history of cancer, SES, leisure-time physical activity and BMI. In an analysis restricted to smokers alone, the relative risk of lung cancer among binge drinking smokers compared with non-binge drinking smokers was 1.79 (95% CI 1.03–3.12) after adjusting for the above (table 2).

In table 3, we carried out a more detailed analysis according to number of cigarettes smoked daily and duration of smoking in years. Among non-smokers, there was no increased risk of lung cancer among binge drinkers, RR 1.48 (95% CI 0.89–2.47), after adjusting for age. Among those who smoked between 1 and 19 cigarettes daily, the RR of lung cancer among binge-drinkers was 2.68 (95% CI 1.63–4.41). Similar increased risks were observed among those who smoked 20–29 cigarettes/day (RR 2.21, 95% CI 1.37–3.70) and those who smoked more than 30 cigarettes daily (RR 2.22, 95% CI
1.34–3.73). Further adjustments for examination year, family history of cancer, SES, leisure time physical activity and BMI did not change the results. The RR for lung cancer among binge drinkers who had smoked for <30 years was 2.76 (95% CI 1.64–4.62) while among those who had smoked for >30 years was 1.72 (95% CI 1.02–2.91) after adjustments for age, examination year, family history of cancer, SES, leisure time physical activity and BMI.

**Discussion**

In this prospective population based study, we found an increased risk of lung cancer only among binge drinking smokers but not among non-smokers. Among smokers, binge drinking was associated with an increased risk of lung cancer irrespective of the number of cigarettes smoked daily or duration of smoking. Even though the number of lung cancer cases among non-smokers was small, the fact that the increased risk was limited to only smokers means that residual confounding by smoking is likely to contribute to the results. Our findings support the fact that men with the highest volume of alcohol consumption appear to be at a higher risk of lung cancer compared with men with low consumption.9,10 Significant dose–response relationship between total alcohol consumption and lung cancer has been reported in some studies.3,4,27–29. Pooled relative risk from a meta-analysis indicates that there is a dose–response relationship between alcohol consumption and lung cancer even after adjusting for smoking.27 In the above meta-analysis, there was a 2% increase in risk among men who consumed 25 g alcohol/day, which increased to 8% among men who consumed 100 g alcohol/day. The European Prospective Investigation into Cancer and Nutrition (EPIC) study however found a non-significant 29% higher risk of lung cancer in people with mean life-long ethanol intake ≥60 g/day compared with people with low mean life-long intake of 0.1–4.9 g/day.8 These findings were similar to those reported by the Framingham study in which there was no significant association between alcohol consumption and lung cancer in the original cohort. This lack of association is likely to be because alcohol consumption among the Framingham cohort was light to moderate and there were few heavy drinkers.7 However, among the Framingham offspring cohort, there was suggestive evidence for an increased risk of lung cancer with alcohol consumption ≥24 g/day.7 Hence, the effects of alcohol on lung cancer risk may be manifest only with high alcohol intake.

Potential mechanisms for the effects of alcohol on lung cancer include carcinogenesis by its main metabolite, acetaldehyde,30 oxidative stress induced by alcohol31,32 and induction by alcohol of cytochrome p450, which affects the metabolism of other pro-carcinogens.33 Binge drinking may promote lung carcinogenesis via biologic mechanisms related to heavy drinking. Heavy drinking compromises liver function which may result in reduced detoxification of carcinogens and reduced delivery of protective nutrients,10 people with genetic polymorphisms that lead to higher internal doses of acetaldehyde following ingestion of alcohol have increased

### Table 1 Baseline characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Binge drinkers</th>
<th>Non-binge drinkers</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>621</td>
<td>1646</td>
<td></td>
</tr>
<tr>
<td>Number of cases</td>
<td>27</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>52.4 (5.2)</td>
<td>53.1 (5.2)</td>
<td>0.09</td>
</tr>
<tr>
<td>Family history of cancer (%)</td>
<td>23</td>
<td>29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Smoking prevalence (%)</td>
<td>10 (12)</td>
<td>8 (5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of smoking (in years)</td>
<td>15.4 (16.3)</td>
<td>7.5 (13.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.8 (4.1)</td>
<td>26.51 (3.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Energy expenditure in leisure time physical activity (kcal/d)</td>
<td>120.2 (147.1)</td>
<td>150.4 (181.8)</td>
<td>0.01</td>
</tr>
<tr>
<td>Vegetables (g), 4 day mean</td>
<td>127.8 (132.6)</td>
<td>168.5 (148.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Fruits and berries (g), 4 day mean</td>
<td>287.4 (126.4)</td>
<td>286.4 (123.)</td>
<td>0.33</td>
</tr>
<tr>
<td>SESb</td>
<td>13.8 (4.8)</td>
<td>11.5 (5.2)</td>
<td></td>
</tr>
<tr>
<td>Weekly alcohol intake (g)</td>
<td>192.4 (222.2)</td>
<td>48.9 (65.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum GGT (UI/L)</td>
<td>41.3 (48.1)</td>
<td>28.4 (35.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean corpuscular volume (fl)</td>
<td>93.4 (5)</td>
<td>91.7 (4.7)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

a: The estimates are computed on current smokers only
b: A higher value of SES index indicates a lower SES

### Table 2 Relative risks for lung cancer among binge drinkers compared with non-binge drinkers in men with no history of lung cancer at baseline

<table>
<thead>
<tr>
<th>Risk ratio</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In whole cohort</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>1.89</td>
<td>1.10–3.20</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.79</td>
<td>1.03–3.12</td>
</tr>
<tr>
<td>Among smokers alone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model 1</td>
<td>1.89</td>
<td>1.10–3.20</td>
</tr>
<tr>
<td>Model 2</td>
<td>1.79</td>
<td>1.03–3.12</td>
</tr>
</tbody>
</table>

Model 1—adjusted for age, examination year, family history of cancer, smoking, SES, leisure time physical activity and BMI
Model 2—adjusted for age, examination year, family history of cancer, life-long cigarette consumption, SES, leisure time physical activity and BMI

### Table 3 Relationship between binge drinking and lung cancer according to smoking categories

<table>
<thead>
<tr>
<th>Cigarette smoking</th>
<th>Number of cigarettes smoked per day</th>
<th>Model 1a</th>
<th>95% CI</th>
<th>P-value</th>
<th>Model 2a</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects (cases)</td>
<td></td>
<td>RR</td>
<td></td>
<td></td>
<td>RR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>1812 (12)</td>
<td>1.48</td>
<td>0.89–2.47</td>
<td>0.13</td>
<td>1.49</td>
<td>0.88–2.56</td>
<td>0.14</td>
</tr>
<tr>
<td>1–19/day</td>
<td>367 (15)</td>
<td>2.68</td>
<td>1.63–4.41</td>
<td>&lt;0.001</td>
<td>2.70</td>
<td>1.61–4.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>20–29/day</td>
<td>329 (22)</td>
<td>2.21</td>
<td>1.33–3.70</td>
<td>0.002</td>
<td>2.35</td>
<td>1.38–3.96</td>
<td>0.002</td>
</tr>
<tr>
<td>≥30/day</td>
<td>119 (16)</td>
<td>2.22</td>
<td>1.34–3.73</td>
<td>0.002</td>
<td>2.24</td>
<td>1.29–3.80</td>
<td>0.004</td>
</tr>
<tr>
<td>Duration of smoking (in years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-smokers</td>
<td>1812 (12)</td>
<td>1.53</td>
<td>0.93–2.52</td>
<td>0.10</td>
<td>1.62</td>
<td>0.96–2.72</td>
<td>0.071</td>
</tr>
<tr>
<td>&lt;30</td>
<td>345 (8)</td>
<td>2.73</td>
<td>1.69–4.48</td>
<td>&lt;0.001</td>
<td>2.76</td>
<td>1.64–4.62</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥30</td>
<td>467 (45)</td>
<td>1.63</td>
<td>0.98–2.70</td>
<td>0.06</td>
<td>1.72</td>
<td>1.02–2.91</td>
<td>0.041</td>
</tr>
</tbody>
</table>

a: Adjusted for age
b: Adjusted for age, examination year, family history of cancer, SES, leisure time physical activity and BMI
risks of alcohol related cancers. Acute intake of alcohol inhibits activity of methionine synthase, this leads to a decreased production of S-Adenosylmethionine ultimately causing global hypomethylation of DNA which is an early feature of neoplastic transformation of epithelial cells. In vivo studies have shown that histone acetylation changes nucleosomal conformation, which increases the accessibility of transcriptional regulatory proteins to chromatin templates, which may therefore induce carcinogenesis. Kim and Shukla demonstrated that acute injection of ethanol in rats analogous to binge drinking induced a 3-fold increase in histone acetylation in lungs and also liver and spleen but not in other organs.

Folate deficiency has been linked with an increased risk of lung cancer. Excessive alcohol intake is also thought to impair bioavailability of folate by diminishing its intestinal absorption and inducing cleavage of its molecule. Binge drinking may be indirectly related to lung cancer by modifying dietary behaviour because heavy drinking has been found to modulate dietary patterns with resultant nutrient deficiency. Dietary factors especially consumption of fruits and vegetables are associated with lower risks of lung cancer. Heavy drinkers are likely to substitute alcohol calories for calories obtained from food and may therefore consume fewer protective foods such as fruits and vegetables. This was observed in our study as binge drinkers consumed less fruits and berries compared with non-binge drinkers but there was no significant difference in their vegetable consumption. Thus, an increased risk of lung cancer among binge drinkers in our study cohort may be due to a combination of the effects of heavy acute alcohol intake, micronutrient deficiency brought about by their drinking pattern, their tendency to smoke more cigarettes and possibly other factors which are not yet known.

Our study raises important health implications. Efforts to reduce incidence of lung cancer may need to consider alcohol drinking pattern within the population. This is especially important in populations where there is a high incidence of binge drinking such as in Finland. Up to 27% of our study subjects engaged in binge drinking. The Finnish alcohol drinking context is characterized by high prevalence of binge drinking sometimes called ‘mythical Finnish boozing’ where almost one in every three drinking occasion results in binge drinking. The prevalence of binge drinking is however higher in the UK with 40% of all drinking occasions ending up in binge drinking.

The strengths of this study include its prospective population based design, reliable assessment of lung cancer and detailed assessment of possible risk factors for lung cancer. The response rate was high, follow-up was long and complete because of the unique personal identifier number in the Finnish population. Assessment of exposure took place at baseline before lung cancer occurred, thereby minimizing recall bias. Men with a history of lung cancer were excluded from the study so it is not likely that participants changed their alcohol consumption pattern before the beginning of study due to pre-existing cancer. We also had a relatively high number of binge drinkers in our cohort. However, the following limitations in our study also need to be considered before drawing conclusions: (i) Alcohol consumption was assessed based on a questionnaire, thus, subject to under-reporting or any other misclassification but we do not expect any bias to be systematically differential across drinking groups. The questionnaire has also been validated in this cohort using biochemical markers of excessive alcohol use such as MCV and GGT (ii) the number of lung cancer cases among non-smokers was low, hence, we may not be able to observe an association between binge drinking and lung cancer among these individuals if one exists. The fact that the association was only evident among smokers means we cannot rule out the residual confounding effects of smoking.

In conclusion, binge drinking is not associated with an increased risk of lung cancer among non-smokers but among smokers, it is associated with an increased risk irrespective of number of cigarettes smoked daily, or duration of smoking. The effects of smoking cannot however be disentangled. This shows that pattern of alcohol consumption may need to be taken into consideration when investigating the association between alcohol and lung cancer because drinking pattern may have independent effects on health not explained by total alcohol consumption.

Acknowledgement

We express gratitude to Kimmo Rainkonen of the Research Institute of Public Health, University of Kuopio for data management.

Funding

Academy of Finland (118551 and 118584) while at the School of Public Health, University of Kuopio.

Conflicts of interest: None declared.

Key points

- No previous study has examined the association between binge drinking pattern and risk of lung cancer.
- Detailed analysis reveals that there was no increased risk among non-smoking binge drinkers. The increased risks were only apparent among smokers, irrespective of amount of cigarettes smoked daily or duration of smoking in years.
- Pattern of alcohol consumption may need to be considered when investigating the association between alcohol and lung cancer.
- Larger studies are needed in order to shed more light on our findings.

References


