

# Alcohol leads on a hepatocellular carcinoma

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## Aim

The present study is based on a literature search, which aims to demonstrate that alcohol can lead on a hepatic cirrhosis and finally on a hepatocellular carcinoma.

## Correlation of alcohol with cirrhosis

Consumption of alcohol affects millions of people worldwide, and it is associated with liver disease mortality and for elevated social and economic costs. Alcoholic liver disease (ALD) can take the form of acute involvement such as alcoholic hepatitis or chronic liver disease such as cirrhosis. The prognosis and severity of ALD depends first of all on the amount and duration of alcohol consumption, secondly on the presence of liver inflammation, thirdly on the diet and the nutritional status and finally on the genetic predisposition of an individual. Additionally, liver cirrhosis is associated with marked morbidity and mortality, the average survival of patient with advanced cirrhosis is 1 to 2 years.<sup>1</sup>

## Correlation of alcohol with cancer

There are several putative risk factors of hepatocellular carcinoma (HCC), with cirrhosis characterizing more than 90% of HCC cases.<sup>2</sup> Cirrhosis is found in 80% of autopsies of patients with HCC, that supports that the majority of patients worldwide with HCC have underlying liver cirrhosis.<sup>3</sup> The risk of developing HCC varies according to the cause of the cirrhosis itself, with alcoholic cirrhosis carrying the greatest risks at 25%.<sup>4</sup> Also, the working group of the International Agency for Research on cancer, based on the association of alcohol with cancer, recently deemed that alcoholic beverages are “carcinogenic to humans,” and that is causally related to occurrence of malignant tumors of liver.<sup>5</sup>

## Hepatocellular carcinoma

Hepatocellular carcinoma (HCC) is considered to be the sixth most common cancer of men and eleventh most common cancer of women worldwide. However, nowadays HCC is the third most common cause of cancer deaths in men and seventh most common in women, because almost every individual who develops hepatic cancer dies of the disease.<sup>6</sup>

## Aim

The aim of the study is to analyze other surveys. Through analyzing other surveys should prove that alcohol can lead to HCC.

## Factors that cause HCC

There are several risk factors that can cause HCC, the most the most common is chronic hepatitis B, which is the dominant risk factor in eastern Asia and sub-saharan Africa. Regarding of developed countries, hepatitis C and alcohol use are the main risk factors. Additionally, in France alcohol is currently the first cause of HCC.<sup>7</sup> The environmental risk factors are associated with tobacco smoking, alcohol intake, obesity and whereas coffee drinking has been reported to reduce the risk of HCC.<sup>8</sup>

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## Incidence of HCC

The geographical distribution of HCC varies greatly worldwide, the areas with the lowest incidence rates include North America, northern Europe and Australia. Although, in the past decades the number of cases of HCC has increased in the United States, United Kingdom, Central Europe, Australia and Japan, with a shift in the incidence rates in the younger age groups. Additionally, rates for liver cancer in men are typically 2 to 4 times higher than in women. Although, the reason for trends are not entirely clear, whether the higher risk of HCC in males reflects an increased susceptibility of men, to the tumor or a greater exposure to environmental risk factors like hepatitis and alcohol.<sup>3</sup>

## Mortality

HCC has a high mortality due to a late diagnosis at an advanced stage. This is the reason why screening of high risk patients is a major issue. Nowadays, the recommendation is to have every patient with cirrhosis a biannual liver ultrasonography, even then only 20% of all HCCs are diagnosed during a surveillance program.<sup>7</sup> Liver cancer is expected to cause 400,00 deaths in a year worldwide, according to this reference liver cancer and especially HCC is a highly fatal disease.<sup>9</sup>

## Treatment

The current treatments in the routine clinical practice for HCC, are first of all surgical resection and secondly liver transplantation, however, these treatments are applicable to only in a small percentage of patients and the prolongation of survival is restricted. Also, there are other treatments besides these two, such as systemic chemotherapy, transcatheter arterial chemoembolization (TACE), cryotherapy, thermotherapy, intra-arterial chemotherapy, percutaneous ethanol injection (PEI), immunotherapy, hormonal therapy, proton therapy or a wide range of their possible combinations. However, there is limited use of these therapies because there is the lack of definitive data. Also, there is another therapy, the gene therapy, which may have a significant role in the future management in HCC.<sup>4</sup>

## Methods

The first survey was conducted in America, by NIH-American Association of Retired Persons Diet and Health Study. It was a case-control study and the aim of the study was to investigate the effect of alcohol consumption and folate intake on HCC incidence and liver disease mortality. The participants were 494,743 people.<sup>10</sup>

The second survey was conducted in eight countries which were participating in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. It was a combination of prospective cohort study with representative population based data on alcohol exposure. The aim of the study was to compute the burden of cancer attributable to current and former alcohol consumption. The participants were 363,988 people, the 109,118 of them were men and the 254,870 were women, and the mainly ages were 37 to 70 years.<sup>11</sup>

The third survey was conducted in 23 centers from 10 European countries which were also, participating in the EPIC. It was a case-control study that aims to investigate the role of biological, dietary, lifestyle and environmental factors in the etiology of cancer and other chronic diseases. The participants were 4409, 809 healthy male and female, from ages 25 to 70 years.<sup>8</sup>

The fourth survey was conducted in Finland, it was a nested case-control study that aims to examine the effects of serum levels of one-carbon metabolite levels and alcohol consumption on the development of liver cancer. The participants were 27,086 Finnish males, with 194 incident liver cancer cases and 213 liver disease deaths.<sup>12</sup>

The fifth survey was conducted in Sweden, and it was a case-control study. The aim of the study was to find environmental factors of possible aetiological importance for primary liver carcinoma (PLC) and HCC. The participants were 102 people, from ages 25 to 80 years.<sup>13</sup>

## Discussion

The first study was a case- control study because we knew if the participants were suffering from HCC and they reported their dietary intake for the previous year. The result of this study was that the consumption of more than three drink of alcohol per day was associated with HCC incidence (hazards ratios HR: 1.92; 95% and confidence intervals CI: 1.42-2.60) and with liver disease mortality HR: 5.84; 95% CI: 4.81-7.10). Also, the survey investigate and folate intake, and the results were that folate can modify the relationship between alcohol and HCC incidence, but it could not modify the relationship between alcohol and liver disease mortality. According to these results folate intake can ameliorate the effect of alcohol consumption on the development of HCC also, it may be beneficial in the prevention of alcohol which is associated with HCC.<sup>10</sup>

The second survey was a cohort study, because we knew that the participants were healthy and they were followed- up for a time-period, while occurring events and outcomes were recorded and associated with exposures. The results of the study were that alcohol is associated with many kind of cancers. The most frequent are the upper aerodigestive tract and the figures were 44% (31 to 56%) in men affected by the cancer of the upper aerodigestive tract, and 25% (5 to 46%) in women. Liver cancer is the second most frequent cancer in the study. The figures were 33% (11 to 54%) of men exhibited in liver cancer and 18% (-3 to 38%) of women. According to this study an important part of the alcohol attributable fraction in 2008 was associated with alcohol consumption higher than the recommended upper limit: 33,037 of 178,578 alcohol-related cancer cases in men and 17,470 of 397,043 alcohol-related cases women. Also, in the western Europe a significant proportion of cancer cases may be due to alcohol consumption, especially when the consumption is higher than the recommended maximum limits.<sup>12</sup>

The third survey was a case- control study, because we knew that the participants were exhibited with the HCC. The results of the study was that the alcohol can lead to a HCC, because 27 from 115 persons with HCC were heavy drinkers. Additionally, heavy alcohol intake contributed (10.2%, 95% CI= -8.6% to 22.5%) in HCC, also the heavy alcohol consumption contributes to the burden of disease.<sup>8</sup>

The fourth survey was also a case- control study, because we knew that the participants were affected by the liver cancer. The results of the study were that the alcohol consumption of more than 20,44 gr per day, was associated with an increased risk of liver cancer incidence (HR 1.52, 95%CI 1.06–2.18) and from liver disease mortality (HR 6.68, 95%CI 4.16–10.71). Also, in the current study were examined and the effects of serum levels of one-carbon metabolite levels, as a result of the examined in the case-control study, was found that none of the serum one-carbon metabolites were associated with liver cancer.<sup>12</sup>

Finally, the fifth survey was also a case- control study. The results of the current study were, that the consuming of spirits more than 370 ml (one bottle) per week was reported that can cause HCC with probability to happened 27/83 (32.5%). The consumption of alcoholic beverages more than 370 ml per month, but less than a bottle weekly, gave a risk ratio for HCC of 2.9 % (X2 = 3.8; C95= 0.99-8.7). Also, a consumption of alcohol maximum of 4 bottles at 370 ml per year, had a risk ratio 2.1 % (x2 = 1.5; CT95 = 0.9-5.1) for HCC, which was not significant.<sup>13,14</sup>

## Conclusion

Based on the results of the five referred studies, alcohol may lead on a liver cancer and on HCC. Also, alcohol is related to carcinogenesis and may interact with other environmental factors such as diet, smoking and co morbidities, and it can also depends on genetic susceptibility.<sup>15</sup>

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## Conflicts of interest

The author declares no conflicts of interest.

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