Hereditary hemochromatosis as an independent risk factor for liver cancer: A matched case-control study of the National Inpatient Sample Database

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Maryam Haider, Ali F. Alsbihi, Zaid Imam, Adnan Malik, Sana Iqbal, Mahum Nadeem, and Ahmed J. Chaudhary
Cox regression analysis of 30 untreated patients revealed that only a high-grade DN was significantly associated with an increased risk of the progression to HCC (P<0.05), as was neither arterial phase enhancement nor size of nodule. Additional immunohistochemical staining of 26 untreated RN or DN specimens identified no significant histologic predictor for HCC development. **Conclusion:** Our findings suggest that more careful and active surveillance for HCC is needed in cirrhotic patients with high-grade DNs in the liver, for which LAT could be considered likely with a preemptive intent. Future studies should focus on the development of biopredictives for malignant transformation of hepatic nodules.

**Disclosures:**
The following people have nothing to disclose: Ji Yoon Kim, Jihye Lim, Dong Man Yu, Ju Hyun Shim
Disclosure information not available at the time of publication: Hyo Jeong Kang

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**HEPATOCELLULAR CARCINOMA IN NON-ALCOHOLIC STEATOHEPATITIS AND CRYPTOGENIC CIRRHOSIS OVER A 15-YEAR PERIOD**

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**Background:** Non-alcoholic steatohepatitis (NASH) has been recognized as the main cause of cirrhosis in patients previously categorized under the term “cryptogenic cirrhosis” (CC). The data regarding similarities and disparities between hepatocellular carcinoma (HCC) patients with either NASH cirrhosis or CC remains limited. We aimed to study the characteristics and trend of biopsy-proven NASH cirrhosis and CC in patients with HCC.

**Methods:** We identified all adult patients with HCC and concomitant diagnosis of NASH-related cirrhosis or cryptogenic cirrhosis who received care at two quaternary liver transplant centers in the United States, between January 2000 and December 2015. Presence of liver cirrhosis was determined based on radiologic and histologic evidence. CC was determined in patients who had no identifiable cause of cirrhosis after extensive clinical, serological and pathological evaluations. Patient with excessive alcohol consumption were excluded. HCC was diagnosed by either pathological diagnosis or radiological diagnosis of Liver Imaging Reporting and Data System (LI-RADS) 5 criteria. Descriptive statistics were presented by mean and standard deviation or median and percentiles for continuous variables and frequencies for categorical variables. Statistical difference between the groups were analyzed using the chi-square test, fisher exact test, student t-test or Mann-Whiney U-test as appropriate.

**Results:** A total of 328 HCC patients were included in the study, 195 patients with biopsy-proven NASH cirrhosis and 133 patients with CC, of which 35 patients had liver biopsy and 98 patients without liver biopsy. Patients with CC were older [69.9±10.2 vs. 66.9±8.4 years; (p=0.004)]. The prevalence of metabolic risk factors, hypertension (71% vs. 69%), diabetes mellitus (67% vs. 59%), and dyslipidemia (47% vs. 41%) in patients with NASH cirrhosis and CC were similar (all P=NS), however, obesity was more prevalent in NASH cirrhosis patients than in CC patients [63% vs. 44% (p=0.001)]. Those with CC had higher median tumor size [5.9 (IQR 3.1, 9.3) vs. 3.5 (IQR 2.6, 5) cm], more extrahepatic metastasis [18.1% vs. 8.2%; (p<0.01)], and were less likely to be within Milan criteria [31.6% vs. 49.7%; (p<0.01)] than patients with NASH cirrhosis. Over the past 15-year period, we found a trend of increasing proportion of patients who would have been classified as cryptogenic cirrhosis being diagnosed with NASH cirrhosis (0% in 2000, 16.7% in 2005, 27% in 2010, and 56.3% in 2015).

**Conclusion:** The prevalence of hypertension, diabetes mellitus, and dyslipidemia in NASH cirrhosis and CC patients with HCC were similar. CC patients were more likely to have more advanced HCC at diagnosis. Finally, there is an increasing trend in NASH cirrhosis and a decreasing trend in cryptogenic cirrhosis in patients with no identifiable cause of liver disease.

**Figure 1.** The prevalence of metabolic risk factors in NASH group, CC group and a subgroup of CC patients with available biopsy data

**Disclosures:**
The following people have nothing to disclose: Kanokwan Pinyopornpanish, Wael Al-Yaman, Miguel Salazar, Gianina Flocco, Ji Seok Park, Arthur J. McCullough

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**HEREDITARY HEMOCHROMATOSIS AS AN INDEPENDENT RISK FACTOR FOR LIVER CANCER: A MATCHED CASE-CONTROL STUDY OF THE NATIONAL INPATIENT SAMPLE DATABASE**

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**Background:** Hereditary hemochromatosis (HH) is a genetic metabolic disorder that increases alimentary iron absorption resulting in the iron overload that can be carcinogenic. In this study, we investigated the carcinogenic potential of HH resulting in liver cancer not only through development of cirrhosis but also in relation to hepatic iron deposition.

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Methods: We conducted a retrospective matched case-control analysis study from National Inpatient Sample (NIS) database between 2016 and 2018. International Classification of Diseases, Tenth Revision (ICD-10) was used to identify patients with a primary or secondary diagnosis of liver cancer (ICD-10 codes C22.0, C22.2, C22.3, C22.4, C22.7, and C22.8). We selected a matched group of patients without liver cancer with the 1:1 fixed ratio nearest neighbor (greedy) propensity score method using the patient’s age, sex, and race. Patients with liver cancer were established as cases, and patients without liver cancer were established as the control group. We also identified established risk factors of liver cancer using ICD-10 codes, including cirrhosis, viral hepatitis, HH (excluding cirrhosis), type 2 diabetes, alcohol, obesity, Tobacco, Non-alcoholic fatty liver disease (NAFLD), and transfusion of blood and blood products. Univariate and multivariate regression analyses were conducted to identify significant correlates of liver cancer. Statistically analysis is performed in RStudio 1.4. P-values < 0.05 demonstrated statistical significance. Results: 34582 patients with liver cancer were identified. Multivariate analyses demonstrated that cirrhosis (aOR, 46.666; 95% CI, 42.659 – 51.050), viral hepatitis (aOR, 13.601; 95% CI, 12.603 – 14.679), hereditary hemochromatosis excluding cirrhosis (aOR, 18.216; 95% CI, 5.348 – 62.045), type 2 diabetes (aOR, 1.613; 95% CI, 1.541 – 1.689), tobacco use (aOR, 1.131; 95% CI, 1.082 – 1.182), NAFLD (aOR, 5.544; 95% CI, 4.709 – 6.528), blood transfusion (aOR, 2.532; 95% CI, 2.334 – 2.746), are independent risk factor of liver cancer. Conclusion: Patients with HH can be at an increased risk for liver cancer independent of cirrhosis status. This may be related to carcinogenic properties of iron deposition related to the disease. More studies are required in controlled settings to further consolidate these findings.

Table 1: Risk Factor Analysis with and without Liver Cancer: NIS 2016 to 2018

<table>
<thead>
<tr>
<th>Variables</th>
<th>Age, Sex, and Race Method</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis</td>
<td>34,582 (35.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Viral Hepatitis</td>
<td>10,265 (10.1%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hereditary Hemochromatosis</td>
<td>15,081 (15.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Type 2 Diabetes</td>
<td>3262 (32.9%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>2281 (5.5%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Tobacco Use</td>
<td>2570 (5.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Alcohol Use</td>
<td>34,582 (35.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NAFLD</td>
<td>34,582 (35.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>34,582 (35.3%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Disclosures:
The following people have nothing to disclose: Maryam Haider, Ali F Alsbihi, Zaid Imam, Adnan Malik, Sana Iqbal, Mahum Nadeem, Ahmed J Chaudhary

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