
Poster 2286

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Background

NAFLD/NASH is projected to be a major cause of mortality in the coming decades.1

1. Although prior studies have found that NAFLD/NASH patient risk of all-cause mortality is higher with increasing fibrosis stage, these studies have not adjusted for patient demographics or comorbidities; nor have they evaluated risk associated with non-severe disease, and have studied a limited number of patients (n=300 in meta-analysis of previous mortality studies).2 3

2. In addition, a recent nationally representative sample of NHANES data reported that the metabolic co-morbidities of diabetes, hypertension, and BMI ≥ 30 kg/m² were independent predictors of significant and advanced fibrosis in NAFLD/NASH patients.4

Aim

1. To evaluate Medicare NAFLD/NASH patients’ risk of all-cause mortality and disease progression, while adjusting for patient demographics and comorbidities, in a real-world cohort.

Study Design and Methods

1. Design: this was a retrospective, observational cohort study.


3. Among NAFLD/NASH patients, 5 study cohorts identified: (1) NAFLD/NASH only patients with no further liver disease progression, (2) compensated cirrhosis (CC) or decompensated cirrhosis (DCC), (3) hepatocellular carcinoma (HCC), (4) liver transplant (LT), (5) the free NAFLD/NASH or advanced liver disease (CC, DCC, HCC, LT) diagnosis marked the index date for all patients. NAFLD/NASH only patients included those with ≥1 diagnosis of liver fatty change (ICD-10-ICM [K76.0, K76.81] codes for NAFLD/NASH aged >18 years between 1/1/2008 and 12/31/2015.

4. All-cause mortality or time to event

5. Inclusion criteria:

6. Exclusion criteria:

   - Patients with other defined causes of liver disease were excluded (cirrhosis, autoimmune liver disease, viral hepatitis, Budd-Chiari syndrome, Wilson disease, autoimmune hepatitis, primary biliary cirrhosis, primary biliary sclerosis, hemochromatosis and primary sclerosing cholangitis).

   - Statistical analyses:

      - Kaplan Meier survival analyses

      - Cox regression models to assess the risk of mortality progression adjusted for patient demographics and comorbidities.

Study Outcomes

1. Outcome - the following were reported for each severity cohort:

   - Baseline demographics and comorbidities

   - All-cause mortality or time to event

Results

Table 1: Patient Selection Flowchart and Disease Severity Groups

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>Number of Patients</th>
<th>Percent of NAFLD/NASH Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAFLD/NASH only</td>
<td>85,535</td>
<td>95.0%</td>
</tr>
<tr>
<td>CC (n=18,500)</td>
<td>9,083</td>
<td>10.4%</td>
</tr>
<tr>
<td>DCC (n=6,487)</td>
<td>4,025</td>
<td>4.6%</td>
</tr>
<tr>
<td>HCC (n=3,114)</td>
<td>1,869</td>
<td>2.1%</td>
</tr>
<tr>
<td>LT (n=3,948)</td>
<td>2,398</td>
<td>2.8%</td>
</tr>
</tbody>
</table>

Table 2: NAFLD/NASH Patient Demographics by Disease Severity

<table>
<thead>
<tr>
<th>Disease Severity</th>
<th>Female, %</th>
<th>Age mean (SD)</th>
<th>Age group, %</th>
<th>Diabetes, %</th>
<th>Dysrhythmia, %</th>
<th>Hypertension, %</th>
<th>Renal impairment, %</th>
<th>Smoking, %</th>
<th>CVD, %</th>
<th>Diabetes mellitus, %</th>
<th>Dysrhythmia, %</th>
<th>Hypertension, %</th>
<th>Renal impairment, %</th>
<th>Smoking, %</th>
<th>CVD, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>NAFLD/NASH only</td>
<td>60.0%</td>
<td>66.0 (11.7)</td>
<td>75-79</td>
<td>46.1</td>
<td>61.5</td>
<td>70.8</td>
<td>60.6</td>
<td>39.4</td>
<td>31.8</td>
<td>29.1</td>
<td>62.3</td>
<td>70.8</td>
<td>20.3</td>
<td>41.3</td>
<td>31.8</td>
</tr>
<tr>
<td>CC (n=18,500)</td>
<td>63.4%</td>
<td>66.8 (10.8)</td>
<td>70-124</td>
<td>39.5</td>
<td>63.6</td>
<td>74.3</td>
<td>53.7</td>
<td>36.3</td>
<td>34.6</td>
<td>34.6</td>
<td>65.7</td>
<td>74.3</td>
<td>27.7</td>
<td>38.2</td>
<td>34.6</td>
</tr>
<tr>
<td>DCC (n=6,487)</td>
<td>53.5%</td>
<td>70.1 (12.4)</td>
<td>70-124</td>
<td>37.8</td>
<td>65.0</td>
<td>76.2</td>
<td>49.5</td>
<td>39.5</td>
<td>37.8</td>
<td>37.8</td>
<td>67.0</td>
<td>76.2</td>
<td>27.7</td>
<td>39.5</td>
<td>37.8</td>
</tr>
<tr>
<td>HCC (n=3,114)</td>
<td>60.7%</td>
<td>73.7 (9.7)</td>
<td>65-79</td>
<td>35.8</td>
<td>64.2</td>
<td>70.5</td>
<td>46.9</td>
<td>40.7</td>
<td>35.8</td>
<td>35.8</td>
<td>66.2</td>
<td>70.5</td>
<td>27.7</td>
<td>42.9</td>
<td>35.8</td>
</tr>
<tr>
<td>LT (n=3,948)</td>
<td>54.0%</td>
<td>72.4 (9.7)</td>
<td>65-79</td>
<td>39.5</td>
<td>65.0</td>
<td>74.3</td>
<td>53.7</td>
<td>36.3</td>
<td>39.5</td>
<td>39.5</td>
<td>65.0</td>
<td>74.3</td>
<td>27.7</td>
<td>41.3</td>
<td>39.5</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meier Survival Analysis of NAFLD/NASH Patients by Cohort

Figure 2. Impact of NAFLD/NASH Patients Liver Disease Severity on Mortality Risk by Cohort

Conclusions

1. This study of Medicare NAFLD/NASH patients found:
   - NAFLD/NASH patients with advanced liver diseases had significantly higher all-cause mortalities than NAFLD/NASH only patients, including higher rates of CVD, DM, and renal impairment.
   - Mortality due to NAFLD/NASH was high and increased from 13% in those with NAFLD/NASH only to 51% in those with CC patients, who also had a significantly higher burden of comorbidities than NAFLD/NASH patients.
   - In the first year following diagnosis, patients’ mortality was over 4 times significantly higher in CC than CC patients and CC-3 times significantly higher in CC than NAFLD/NASH patients. This trend remained after adjustment for patient demographics and comorbidities.
   - Over the 8 year study period, the probability of liver disease progression in NAFLD/NASH patients to CC or more severe disease was 39% and progression in patients with CC due to NAFLD was 45%.
   - Early identification and effective treatments for NAFLD/NASH patients are needed to reduce the rate of mortality.

Limitations

1. NAFLD/NASH patient group may include F0-F3 patients as well as undiagnosed F4 (CC) patients who are under coding limit and lack of ICD codes for F0-F3.

2. Results are limited to the US Medicare population.

3. As with all claims databases, these data were subject to data coding limitations, data entry error, and misclassification of NAFLD/NASH.

4. Results characterized all-cause mortality rather than liver-specific mortality.

Disclosures

1. Sponsored by Gilead Sciences, Inc. Tel: (650) 574-3000