Optimizing I/E Criteria for Early NASH Clinical Studies with FibroScan®

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Introduction

- Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are the hepatic manifestation of metabolic syndromes. NASH is a chronic, progressive disorder that can lead to cirrhosis, end-stage liver disease, and even hepatocellular carcinoma.
- Currently there is no FDA-approved treatment for NASH; however, there are over 90 investigational drugs in development to treat this disease.

Figure 1. The natural history and prevalence of NAFLD/NASH.

Recent studies show the FibroScan has good performance for identifying fibrosis measured with FibroScan®. Specifically, the concordance between FibroScan CAP and TG as well as VCTE and ALT and FIB-4 were examined.

Methods

- More than 200 subjects participated in the pre-screening at Celerion clinics in Tempe AZ and Lincoln, NE.
- The screening event consists of simple anthropometric measurements, fasting blood sample for clinical labs and FibroScan assessment. Transient elastography and CAP measurements were performed with the FibroScan Touch 502 device using M or XL probes.
- Eligible participants are ≥18 (or ≥19 in Lincoln) years of age with a BMI ≥30 kg/m².

Results

Based on the specified cutoffs for TG, ALT and FIB-4, 31%, 20% and 10% of the study population displayed elevated values respectively. Fatty liver and liver stiffness were observed in 78% and 28% of the study group respectively.

Table 1. Participant characteristics.

<table>
<thead>
<tr>
<th>Trait</th>
<th>CAP&lt; 3.0 kPa</th>
<th>CAP≥ 3.0 kPa</th>
<th>ALT&lt;43 IU/L</th>
<th>ALT≥43 IU/L</th>
<th>FIB4&lt; 1.33</th>
<th>FIB4≥ 1.37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>46.1±11.3</td>
<td>50.3±13.2</td>
<td>44.7±14.2</td>
<td>52.2±13.7</td>
<td>43.9±16.1</td>
<td>50.8±13.9</td>
</tr>
<tr>
<td>Female</td>
<td>116/189</td>
<td>114/185</td>
<td>113/182</td>
<td>114/185</td>
<td>115/188</td>
<td>117/188</td>
</tr>
<tr>
<td>BMI</td>
<td>32.4±6.4</td>
<td>36.4±6.7</td>
<td>32.7±5.4</td>
<td>36.3±7.2</td>
<td>34.1±8.0</td>
<td>35.3±6.0</td>
</tr>
<tr>
<td>Platelet (10⁹/L)</td>
<td>229±110</td>
<td>234±109</td>
<td>241±115</td>
<td>230±106</td>
<td>239±112</td>
<td>239±110</td>
</tr>
<tr>
<td>FIB4</td>
<td>0.9±0.8</td>
<td>1.5±1.2</td>
<td>0.8±0.7</td>
<td>1.4±1.1</td>
<td>0.8±0.7</td>
<td>1.4±1.1</td>
</tr>
</tbody>
</table>

Table 2. Contingency analysis.

<table>
<thead>
<tr>
<th>Trait</th>
<th>CAP&lt; 3.0 kPa</th>
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<th>ALT&lt;43 IU/L</th>
<th>ALT≥43 IU/L</th>
<th>FIB4&lt; 1.33</th>
<th>FIB4≥ 1.37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>20/100</td>
<td>17/100</td>
<td>20/100</td>
<td>17/100</td>
<td>20/100</td>
<td>17/100</td>
</tr>
<tr>
<td>Negative</td>
<td>180/200</td>
<td>183/200</td>
<td>179/200</td>
<td>184/200</td>
<td>180/200</td>
<td>183/200</td>
</tr>
</tbody>
</table>

Discussion & Conclusion

- Fatty liver determined by CAP was identified in nearly 60% of the study group, which is consistent with other population-based studies [8]. Elevated TG levels were observed in 1/3 of the cohort, resulting in a PPV of 88%.
- ALT and FIB-4 demonstrated lower PPV at 42% and 44% respectively, with low concordance determined by the likelihood ratio.
- Taken altogether, elevated clinical labs may adequately reflect a NAFLD/ NASH population for early clinical studies, however imaging modalities such as the FibroScan can optimize study pre-screening. FibroScan is a reproducible, quick and painless procedure that can be easily integrated into screening events.
- Moreover, recent FDA draft guidance indicates that early phase inclusion criteria for NASH studies may include biochemical clinical lab) characterizations with imaging assessments[7].
- Therefore, FibroScan assessment of liver fat and stiffness may be a more applicable I/E criteria for early clinical NAFLD/NASH studies than traditional labs alone.

References


Acknowledgments

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