Fibrogenesis

Examining the Relationship Between Atherogenic Indices and the Non-Invasive Fibrosis Biomarker FIB4

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INTRODUCTION

- Nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) are the hepatic manifestation of metabolic syndrome. NASH is the most common form of chronic liver disease in Westernized society, leading to cirrhosis and end-stage liver disease (Figure 1).

- The FIB4 index is a non-invasive biomarker used to identify NASH patients at risk of advanced fibrosis. The index was developed to stage liver disease in subjects with HIV-hepatitis co-infection [5], and more recently has been applied as a marker of fibrosis in NASH [2].

- NASH/NASH is also an independent risk for cardiovascular disease (CVD) [3]. However, the risk of dyspnea in NASH is not well understood, especially in patients with advanced fibrosis.

- A recent large cross-sectional study of approximately 12,000 adults revealed that advanced hepatic fibrosis was associated with reduced TG levels [10].

- Pharmacological reversal of steatohepatitis improved TG and HDL cholesterol levels but not LDL levels [10].

- Atherogenic indices are markedly higher in NASH children with advanced hepatic fibrosis compared to pediatric subjects with no or mild fibrosis [6].

- Atherogenic indices such as LDL/HDL and triglyceride levels are similar to those observed in pediatric subjects with no or mild fibrosis [6].

RESULTS

- A FIB4 cutoff value of 1.3 was applied to identify potential NASH subjects [2]. A sensitivity of 84% and specificity of 69% were observed for the FIB4 test [11].

- Atherogenic indices are markedly higher in NASH children with advanced hepatic fibrosis compared to pediatric subjects with no or mild fibrosis [6].

- Atherogenic indices such as LDL/HDL and triglyceride levels were similar between the two groups.

METHODS

- The dataset for the exploratory analysis was created using screening clinical laboratory results from ClinQuick®, Celerion’s proprietary electronic data acquisition system.

- Main subjects, 30-70 years old, with a BMI >25 kg/m² were identified from a pool of laboratory results from ClinQuick®, Celerion’s proprietary electronic data acquisition system.

- Subjects were generally healthy and the majority had liver function tests within 1.5x ULN.

- Data should be confirmed in a larger population with inclusion of both genders. Subjects were generally healthy and the majority had liver function tests within 1.5x ULN.

- FIB4 index = Age (years) × AST (U/L) / (Platelet count [×10^9] + ALT (U/L)).

- Significant p-value was set at p<0.05, where NS indicates not significant.

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- Pharmacological reversal of steatohepatitis improved TG and HDL cholesterol levels but not LDL levels [10].

- Although NASH subjects with advanced fibrosis are at greater risk of CVD [3], simple atherogenic indices may not reflect this prospect in an adult NASH cohort.

- Early clinical NASH/FIB4 studies with small cohort size may benefit from the incorporation of more sensitive biomarkers, such as peroxisomal proliferator-activated receptor (PPAR) and arterial stiffness [15], to monitor CVD risk factors.

DISCUSSION & CONCLUSION

- The FIB4 index did not correlate with the atherogenic markers however, a significant association between ALT levels and LDL/HDL and HDL were observed. This finding is consistent with results from Siddiqui et al. demonstrating ALT positivity correlated with CVD risk factors such as a percent small dense LDL (LDLb) and VLDL size [10].

- While this was an exploratory investigation, a number of study limitations must be addressed:

- Fibrates were not established by liver biopsy or imaging modalities such as magnetic resonance elastography (MRE) or FibroScan®.

- Results should be confirmed in a larger population with inclusion of both genders.

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REFERENCE


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