Liver Fat Isn’t the True Culprit Behind NASH-Related Disease Progression

The actual cause was discovered during the failed trial of a non-alcoholic steatohepatitis (NASH) treatment.

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Liver fat content does not drive disease progression among people with non-alcoholic steatohepatitis (NASH); rather, fibrosis, or scarring of the organ, is the culprit, MedPage Today reports. Researchers reached this conclusion during otherwise failed placebo-controlled trials of a treatment for NASH, the cloned antibody simtuzumab.

Between the two trials, investigators enrolled 477 people with NASH, including 219 people with bridging fibrosis and 258 with cirrhosis, to receive a planned 240 weeks of simtuzumab.

At the 96-week mark of the trials, the treatment showed no efficacy and the studies were discontinued.

The research was not for naught, however, as the researchers discovered that having advanced fibrosis or cirrhosis was the most important predictor of NASH-related clinical outcomes among the study population.

After a median 25 months of follow-up, 21.5 percent (47 people) of those with bridging fibrosis developed cirrhosis. Factors related to fibrosis predicted such liver-disease progression; these factors included liver collagen and enhanced liver fibrosis (ELF) score at the study’s outset. Liver fat–related measures at the beginning of the study did not predict progression to cirrhosis; these measures included NAFLD (non-alcoholic fatty liver disease) Activity Score (NAS), steatohepatitis, lobular inflammation and hepatocyte ballooning.

These findings applied similarly to the prediction of who among those with cirrhosis would experience a major clinical event related to liver disease. After a median 27 months of follow-up, 19 percent (49 people) of those with cirrhosis experienced ascites, variceal bleeding, new varicies, hepatic encephalopathy, an increase in Child-Pugh or Model for End-Stage Liver Disease (MELD) score, or death.

Among those with cirrhosis, an Ishak fibrosis stage of 5 versus 6 did not impact the development of such clinical events; however, the change in this stage over time was linked to a risk of such

events. Having a higher hepatic collagen and ELF score at the study's outset, and experiencing a worsening of these measures over time, predicted clinical events. Initial levels of NAS , steatohepatitis, lobular inflammation and hepatocyte ballooning did not have such predictive value.

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