Starting HIV Treatment Improves Liver Fibrosis

Regardless of whether individuals have hepatitis B or C, the improvement tends to occur quickly.

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People who begin antiretroviral (ARV) treatment for HIV generally see their liver fibrosis (scarring) improve, including those with and without hepatitis B or C viruses (HBV/HCV). The improvement tends to occur during the first few months of ARV treatment, while worsening of liver damage tends to come later and progress over years.

Chinese researchers conducted a retrospective cohort study of HIV-positive individuals starting ARVs in Yunnan, China. They sought to assess the effect of ARV initiation on long-term changes of liver fibrosis according to the Fibrosis-4, or FIB-4, system of scoring the severity of liver damage.

The scientists published their findings in the Journal of Viral Hepatology.

FIB-4 takes into account age, AST liver enzyme level and platelet count. For the purpose of this study, the investigators broke the scoring system into three categories: Class 1 was a FIB-4 score less than 1.45, meaning no significant fibrosis; Class 2 was a score between 1.45 and 3.25, meaning moderate fibrosis; and Class 3 was a score greater than 3.25, meaning severe fibrosis.

The researchers defined improvement in fibrosis as a change in an individual’s baseline (initial) class to a lower class during follow-up. Conversely, fibrosis progression was defined as a change to a higher class relative to baseline during follow-up.

Data on the study participants came from the Chinese Comprehensive Response Information Management System (CRIMS), a unified web-based national information system that facilitates long-term assessment of health data.

The study’s final analysis included 3,900 people with HIV who started ARVs between January 2004 and March 2015 and who were observed for at least one year through March 31, 2016, at the latest. They were at least 16 years old upon starting ARVs and had the necessary test results to determine HBV and HCV status as well as to calculate FIB-4 score at baseline and at least two follow-up visits, including one during the first 12 months after starting ARVs. Those with platelets higher than 40,000 per milliliter were excluded.
Out of the overall study cohort, 2,675 (68.6 percent) had HIV only, 208 (5.3 percent) were coinfected with HBV (meaning they had the liver virus in addition to HIV), 929 (23.8 percent) were coinfected with HCV and 88 (2.3 percent) were coinfected with both HBV and HCV. The overall group had a median age of 35.6; 60.7 percent were male; 27.1 percent contracted HIV through injection drug use; 72.9 percent contracted the virus through sex or some other route; the median time between HIV diagnosis and starting ARVs was 1.3 years; and the median CD4 count at baseline was 260.

The study cohort members were followed for a median 3.3 years. A respective 52.6 percent and 74.2 percent of those in Class 2 and Class 3 experienced a change to a lower fibrosis class during follow-up; both of these shifts occurred more frequently in those who had only HIV (known as being HIV monoinfected) compared with those who were coinfected with HBV, HCV or both. The median time between starting ARVs and experiencing a shift to a lower fibrosis class was one month. Statistical analysis showed that the HIV-monoinfected group had the fastest rate of change to a lower fibrosis class than the other three groups.

After adjusting the data for various factors, the study authors found that being older, being male, having contracted HIV through injection drug use, having HCV coinfection and taking Viread (tenofovir disoproxil fumarate, or TDF, which is used as both HIV and HBV treatment) were all negative predictors for a change to a lower fibrosis class. Positive predictors for changing to a lower fibrosis class included being in Class 3 at baseline (compared with being in Class 2) and having greater increases in CD4 count over time.

A respective 12.8 percent and 5 percent of those in Class 1 and Class 2 experienced a change to a higher fibrosis class during follow-up; both shifts occurred more frequently in the two groups of people with HCV. The median time from ARV initiation to a change to a higher fibrosis class was 5.7 months. Statistical analysis showed that the two groups with HCV had the faster rates of change to a lower fibrosis class compared with the other two groups without HCV.

After adjusting the data for various factors, the researchers found that being older, being male and having HCV were positive predictors of shifting to a higher fibrosis class. Negative predictors of progressing to a higher fibrosis class included being in Class 2 at baseline (compared with being in Class 1) and having a baseline CD4 count of 350 or greater.

The study authors categorized changes in fibrosis classes according to the following codes: G0 was no change in classes during follow-up; G1 was a change to a lower class only; G2 was a change to a higher class only; and G3 was a combination of a change to a lower class and a change to a higher class.

Among the entire study cohort, the estimated median FIB-4 score showed an overall downward trend after ARV initiation regardless of HBV or HCV coinfection status. The estimated median FIB-4 score over time for the 981 individuals in G1 was similar to that of all cohort members; however, they experienced a steeper increase in liver disease severity during their first two years on ARVs. The estimated median FIB-4 score for the 345 people in G2 increased steadily after they started
ARVs and continued until the five-year mark, with particularly steep increases among those with HCV.

A total of 194 (5 percent) of the study members died during follow-up, including 48 who died of AIDS-related causes. The median time between ARV initiation and death was 3.1 years. Among those who began the study in Class 1, 15 (5.2 percent) of those ultimately classified as G2 died, compared with 55 (2.1 percent) of those in G0. Among those in Class 2, 32 (6.9 percent) of those in G1 died, compared with 27 (4.5 percent) in G0 and nine (15.8 percent) in G2. Among those in Class 3, 35 (9.2 percent) in G1 died compared with 21 (15.9 percent) in G0.

After adjusting the data to account for differences in baseline FIB-4 class, a change to a lower class had marginally statistically significant association with a lower risk of death in those with a baseline FIB-4 of greater than 3.25. (If an association is deemed statistically significant, it is unlikely to have occurred by chance; conversely, if it is not statistically significant, it likely occurred by chance.) This association was statistically significant, however, with regard to non-AIDS-related death.

The study authors said a key finding of their research was that ARV treatment is associated with an overall reduction in liver fibrosis regardless of HBV and HCV coinfection status. Additionally, most changes to a lower FIB-4 status occur during the first three months of ARV treatment and persist during follow-up, while shifts to a higher FIB-4 class tend to develop later and worsen over time. A third key finding was that recovering CD4 cells and suppressing HIV through ARV treatment protect against liver fibrosis progression, while being older, male, having HCV coinfection and taking Viread are risk factors.

To read the study abstract, click here.