Original Investigation

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Association of Direct-Acting Antiviral Therapy With Liver and Nonliver Complications and Long-term Mortality in Patients With Chronic Hepatitis C

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Key Points

Question What is the risk of mortality and liver and nonliver complications for patients with chronic hepatitis C (CHC) who are being treated with direct-acting antivirals (DAAs)?

Findings This cohort study of 245 596 adults with CHC found that DAA treatment (vs no treatment) was independently associated with a lower risk of mortality and liver (ie, hepatocellular carcinoma and decompensation) and nonliver (ie, diabetes, chronic kidney disease, cardiovascular disease, and non-liver cancer) outcomes.

Meaning These findings support the need for continued efforts to promote hepatitis C screening for diagnosis and treatment of CHC before onset of complications to prevent liver and nonliver complications and to lower all-cause mortality.

Abstract

Importance Chronic hepatitis C (CHC) and its complications are associated with high rates of morbidity and mortality. However, large-scale data analysis of the long-term liver and nonliver effects of direct-acting antiviral (DAA) treatment has been limited.

Objective To assess the association of hepatitis C virus elimination through DAA treatment with the risk of liver and nonliver morbidity and mortality during long-term follow-up among a large nationwide

cohort of insured patients with CHC in the US.

Design, Setting, and Participants This was a retrospective cohort study of 245 596 adult patients with CHC using data from the Optum Clinformatics Data Mart database, 2010 to 2021. Of the total cohort, 40 654 patients had received 1 or more prescriptions for DAA medication (without interferon), and 204 942 patients were untreated.

Exposure Treatment with a DAA.

Main Outcomes and Measures Incidence of hepatocellular carcinoma (HCC), liver decompensation, relevant nonliver events (nonliver cancer, diabetes, chronic kidney disease, cardiovascular disease), and overall mortality.

Results The DAA-treated cohort (vs untreated) were older (mean [SD] age, 59.9 [10.8] vs 58.5 [13.0] years; $P < .001$); more likely to be male (25 060 [62%] vs 119 727 [58%] men; $P < .001$) and White (23 937 [59%] vs 115 973 [57%]; $P < .001$) individuals; and more likely to have diabetes (10 680 [26%] vs 52 091 [25%]; $P < .001$) or cirrhosis (17 971 [44%] vs 60 094 [29%]; $P < .001$). Comparing DAA-treated with untreated patients, the incidence (per 1000 person-years) of liver outcomes (eg, decompensation, 28.2 [95% CI, 27.0-29.4] vs 40.8 [95% CI, 40.1-41.5]; $P < .001$, and HCC in compensated cirrhosis, 20.1 [95% CI, 18.4-21.9] vs 41.8 [95% CI, 40.3-43.3]; $P < .001$) and nonliver outcomes (eg, diabetes, 30.2 [95% CI, 35.4-37.7] vs 37.2 [95% CI, 36.6-37.9]; $P < .001$; and chronic kidney disease, 31.1 [95% CI, 29.9-32.2] vs 34.1 [95% CI, 33.5-34.7]; $P < .001$) were significantly lower in treated patients. The all-cause mortality rates per 1000 person-years were also significantly lower in DAA-treated compared with untreated patients (mortality, 36.5 [95% CI, 35.4-37.7] vs 64.7 [95% CI, 63.9-65.4]; $P < .001$). In multivariable regression analysis, DAA treatment was independently associated with a significant decrease in the risk of liver (adjusted hazard ratio [aHR] for HCC, 0.73; decompensation, 0.36), nonliver (aHR for diabetes, 0.74; chronic kidney disease, 0.81; cardiovascular disease, 0.90; nonliver cancer, 0.89), and mortality outcomes (aHR, 0.43).

Conclusions and Relevance The findings of this retrospective cohort study indicate that DAA treatment for insured patients with CHC was associated with improved liver- and nonliver outcomes, and ultimately, with long-term overall survival.

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