IMPACT OF DIRECT-ACTING ANTIVIRAL TREATMENT ON MORTALITY RELATED TO EXTRAHEPATIC MANIFESTATIONS: FINDINGS FROM A LARGE POPULATION-BASED COHORT IN BRITISH COLUMBIA, CANADA

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Background:
Chronic hepatitis C virus (HCV) infection is associated with mortality due to extrahepatic manifestations (EHM). The sustained virologic response (SVR) following the highly effective direct-acting antivirals (DAA) has been linked to decreased all-cause and liver-related mortality. However, evidence on the impact of DAA on EHM-related mortality is lacking.

Methods:
The British Columbia (BC) Hepatitis Testers Cohort includes ~1.3 million people tested for HCV and is linked with various administrative health data. We compared three groups of individuals: treated & SVR, treated & no-SVR, and untreated. EHM-mortality included deaths due to diabetes, rheumatoid arthritis, cardiovascular, cerebrovascular, renal and neurocognitive diseases. Eligible individuals were followed to the earliest of 1) EHM-related-death; 2) other death, or 3) end of study (2019/12/31). To adjust for differences in baseline characteristics, we estimated the inverse probability of treatment weights (IPTW). Then, we used IPTW-weighted multivariable subdistributional hazards model adjusting for competing risk and confounders.

Results:
Study population included 10,694 treated (10,254 SVR, 440 no-SVR) and 10,694 untreated individuals. Among untreated people, 44.4% had history of injection drug use (IDU). Among those who received treatment, 33.4% of those with SVR and 50.9% of those with no-SVR had history of IDU. EHM-mortality rate was 5.86 per 1,000 PYFU (95% confidence interval [CI] 5.00-6.87) for treated & SVR; 25.32 per 1,000 PYFU (95% CI 16.67-38.45) for treated & no-SVR; and 29.40 per 1,000 PYFU (95% CI 27.21-31.76) for untreated individuals. In multivariable model, treated & SVR group had the greatest reduction in EHM-mortality (adjusted hazard ratio [aHR] 0.16, 95% CI 0.13-0.20), followed by treated & no-SVR group (aHR 0.57, 95% CI 0.34-0.94) compared to untreated group.

Conclusion:
Virologic cure of HCV following DAA treatment was associated with a significant reduction in EHM-mortality. This highlights the crucial need of providing diagnosis and treatment for people living with HCV infection to reduce extrahepatic mortality.

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