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Overall mortality in patients with chronic hepatitis C: major effects of social vulnerability, tobacco smoking, and history of unhealthy alcohol use (ANRS CO22 HEPATHER cohort)

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Background and aims: The advent of direct acting antivirals has paved the way for a hepatitis C-free world. However, patients with hepatitis C virus (HCV) infection remain at high risk of morbidity and mortality, even after cure. We identify socio-behavioural factors associated with overall (i.e., all-cause) mortality in chronic HCV-infected patients.

Method: We used data collected from August 2012 to June 2018 in the French, multicentre, prospective cohort ANRS CO22 HEPATHER. The study sample comprised chronic HCV-infected patients who attended at least one annual follow-up visit. Analyses focused on the first five years of follow-up. Socio-behavioural data were collected at cohort enrolment (questionnaire administered by a physician). Living in poverty was defined as a standard of living below 1015€ (French poverty threshold in 2015), low educational level as level <high school diploma, unhealthy alcohol use as drinking >2 and >3 alcohol units/day for women and men, respectively, and elevated coffee intake as drinking ≥3 cups of coffee/day. Factors associated with overall mortality were identified using a Cox proportional hazards model. Adjusted population attributable fractions (PAF) were estimated for the modifiable factors of the multivariable analysis.

Results: Of the 10,366 patients in the study sample, 697 died during follow-up. After multivariable adjustment (for sex, age, educational level, HCV genotype, HCV transmission category, and HCV cure), living in poverty (adjusted hazard ratio [aHR]: 1.34 [95% confidence interval, 1.13–1.60]), tobacco smoking (1.70 [1.35–2.14]), and a history of unhealthy alcohol use (1.48 [1.18–1.86]) were independently associated with increased overall mortality. By contrast, elevated coffee intake was associated with lower overall mortality (0.63 [0.52–0.77]). The risk factors accounting for the greatest mortality burden were tobacco smoking, low educational level, living in poverty, and a history of unhealthy alcohol use (PAF: 16.6%, 14.9%, 9.8%, and 7.4%, respectively), whilst HCV cure and elevated coffee intake averted a high proportion of deaths (86.0% and 13.4%, respectively).

Conclusion: In the era of HCV cure, tobacco cessation must be further encouraged in patients with chronic HCV infection, as a modifiable risk factor of mortality. Specific interventions should be developed to target socially vulnerable patients and those with a history of unhealthy alcohol use, who are at higher risk of mortality.

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Is routine Ribavirin mandatory for genotype 3 hepatitis C compensated cirrhosis patients receiving Sofosbuvir/Velpatasvir? A meta-analysis

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Background and aims: Simplified treatment regimen is crucial for rapid treatment upscale to achieve hepatitis C virus (HCV) elimination. Addition of ribavirin (RBV) to Sofosbuvir/Velpatasvir (SOF/VEL) has been showed improved sustained virological response at 12 weeks (SVR12) in genotype 3 (GT3) decompensated cirrhosis patients. However, the benefits of RBV in GT3 compensated cirrhosis patients receiving SOF/VEL, remains unclear. We aim to systematically review the efficacy and safety of SOF/VEL, with or without RBV in GT3 compensated cirrhosis patients.

Method: With help of medical librarian, we systemically searched four electronic databases (PubMed/MEDLINE, EMBASE, Cochrane Library and Web of Science) from inception up to June 2021 using both free text and MeSH terms. There was no restriction on language, geography, publication dates and publication status. All GT3 compensated cirrhosis patients treated with 12 weeks of SOF/VEL, with or without RBV, were included, regardless of age, gender or prior treatment experience. The primary outcome was the SVR12. The secondary outcome was treatment-related adverse events, as defined by symptomatic anaemia requiring transfusion or a drop in haemoglobin beyond 2 g/dL. The pooled relative risk (RR), 95% confidence interval (CI) and heterogeneity (I^2) were estimated using Review Manager Version 5.3.

Results: From 1,752 citations, a total of 7 studies (2 RCTs, 5 cohort studies) with 1,088 subjects were identified. The SVR12 was similar in GT3 compensated cirrhosis patients, regardless of the use of RBV, for both the intention-to-treat (RR: 1.03, 95%CI: 0.99–1.07; $I^2 = 0\%$) and the per-protocol analysis (RR: 1.03, 95%CI: 0.99–1.07; $I^2 = 48\%$). The overall pooled rate of treatment-related adverse events was 7.2%. Addition of RBV was associated with 4-fold higher risk of treatment-related adverse events in GT3 compensated cirrhosis patients receiving SOF/VEL (RR: 4.20, 95%CI: 1.29–13.68; $I^2 = 0\%$). Subgroup analysis showed that RBV was associated with a numerically higher SVR12 (96% vs 87%, $p = 0.12$) in GT3 compensated cirrhosis patients with baseline resistance-associated substitutions (RAS). However, addition of RBV did not significantly increase the SVR12 among treatment-experienced GT3 compensated cirrhosis patients.

Conclusion: Ribavirin did not significantly increase the SVR12 in GT3 compensated cirrhosis patients receiving SOF/VEL. Our findings suggest limited role for RBV as routine add-on therapy to SOF/VEL in GT3 compensated cirrhosis patients.

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High frequency of hepatitis C virus reinfection following antiviral treatment in the North East of England

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Background and aims: Hepatitis C virus infection (HCV) is common, and injecting drug use (IDU) is the major risk factor for acquisition in