All-cause mortality and causes of death in the Swiss Hepatitis C Cohort Study (SCCS)

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BACKGROUND

- With the introduction of direct-acting antiviral agents (DAA), morality rates and causes of death among persons with Hepatitis C infection are likely to change over time. However, the emergence of such trends may be delayed by the relatively slow progression of the disease.
- To date, detailed analyses of cause-specific mortality among HCV-infected persons over time remain limited.

METHODS

- We evaluated changes in causes of death, between 2008 and 2016, among participants to the SCCS, a prospective observational cohort of confirmed HCV-infected adults in Switzerland.
- We analysed risk factors for all-cause and cause-specific mortality, using Cox Proportional Hazard Regression including time-dependent covariables.
- Mortality ascertainment in the SCCS was completed by linking dead and lost-to-follow-up participants to the Swiss Federal Statistical Office (SFSO) death registry.

Leading causes of deaths evolved over time, with an increasing proportion of cancer-related deaths.
The positive impact of DAA is not observable yet, due to both the slow progression of chronic hepatitis C and the progressive relaxation of guidelines for using those new drugs

RESULTS

- 4,700 SCCS participants were included, of whom 478 died between 2008 and 2016
- Linkage to the SFSO death registry allowed to decrease substantially the proportion of deaths with unknown causes, from 42% to 10%.
- Leading causes of death were liver failure, liver cancer and non-liver cancer, with an increasing proportion of cancer-related deaths over time (Figure 1).
- Cause-specific analysis showed that persons with sustained virologic response (SVR) were less at risk for liver-related mortality than those never treated or those treated unsuccessfully.

CONCLUSIONS

- Although the expected decrease in mortality is not yet observable, causes of death among HCV-infected persons evolved over time.
- With the progressive widening of guidelines for DAA use, liver-related mortality is expected to decline in the future.
- Continued monitoring of cause-specific mortality will remain important to assess the long-term effect of DAA and to design effective interventions.

ADDITIONAL INFORMATION

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	Total: 4700 persons	All–cause (478 deaths)
Sex		P < 0.001
	Male	1
	Female	0.68 (0.56 – 0.84)
Age at start (yr)		P < 0.001
	20	0.59 (0.37 – 0.96)
	40	1
	60	2.52 (2.04 – 3.11)
Treatment status		P < 0.001
	Never treated	1
	Treated with DAA, SVR	0.23 (0.08 – 0.63)
	Treated with DAA, failure	0.94 (0.33 – 2.66)
	Treated with IFN, SVR	0.33 (0.24 – 0.45)
	Treated with IFN, failure	0.87 (0.71 – 1.07)
Fibrosis score		P < 0.001
	F0, F1 or F2	1
	F3 or F4	3.57 (2.9 – 4.38)
IDU		P < 0.001
	Never	1
	Ever	2.01 (1.57 – 2.58)

Estimates of the effect of gender, age, treatment, fibrosis stage and IDU on mortality, from Cox regression models

	Total: 4700 persons	Liver failure (114 deaths, 23.8%)	Liver cancer (89 deaths, 18.6%)	Non–liver cancer (72 deaths, 15.1%)	Cardiovascular (33 deaths, 6.9%)	Unnatural cause (65 deaths, 13.6%)
Sex		P = 0.15	P = 0.09	P = 0.074	P = 0.041	P = 0.18
	Male	1	1	1	1	1
	Female	0.73 (0.48 – 1.12)	0.66 (0.41 – 1.07)	0.61 (0.36 – 1.05)	0.44 (0.2 – 0.97)	0.68 (0.39 – 1.19)
Age at start (yr)		P = 0.016	P < 0.001	P < 0.001	P < 0.001	P = 0.044
	20	0.26 (0.08 – 0.89)	0.08 (0.01 – 0.62)	0.05 (0.01 – 0.28)	0.65 (0.08 – 5.62)	2.92 (1.23 – 6.96)
	40	1	1	1	1	1
	60	2.1 (1.27 – 3.48)	6.32 (2.74 – 14.57)	8.5 (4.03 – 17.92)	5.23 (2.05 – 13.31)	1.04 (0.59 – 1.84)
Treatment status		P < 0.001	P < 0.001	P = 0.29	P = 0.16	P = 0.12
	Never treated	1	1	1	1	1
	Treated with SVR	0.18 (0.08 – 0.38)	0.32 (0.15 – 0.7)	0.6 (0.32 – 1.14)	0.39 (0.14 – 1.11)	0.47 (0.23 – 0.97)
	Treated with failure	0.8 (0.53 – 1.2)	1.37 (0.83 – 2.26)	0.83 (0.46 – 1.5)	0.62 (0.26 – 1.45)	0.92 (0.5 – 1.7)
Fibrosis score		P < 0.001	P < 0.001	P = 0.11	P = 0.0064	P = 0.024
	F0, F1 or F2	1	1	1	1	1
	F3 or F4	12.67 (7.22 – 22.24)	13.75 (6.49 – 29.17)	1.51 (0.91 – 2.51)	2.91 (1.35 – 6.27)	1.96 (1.09 – 3.5)
IDU		P = 0.25	P = 0.19	P < 0.001	P = 0.2	P = 0.0013
	Never	1	1	1	1	1
	Ever	1.32 (0.82 – 2.11)	1.47 (0.83 – 2.62)	3.33 (1.68 – 6.6)	2.01 (0.7 – 5.78)	3.57 (1.64 – 7.77)

Figure 1: Cumulative incidence of causes of death over time since registration in the SCCS

