AASLD 2013: Long term survival of liver fibrosis after virological cure (SVR) in patients with chronic hepatitis C (CHC): The avenue of the scars?

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Background:
CHC is both a virologic and a fibrotic disease and complications can occur in SVR pts with residual fibrosis. Due to the burden of repeated biopsies, no study has been done on the long-term outcome of fibrosis after SVR in a large population. FibroTest (FT) has been validated as a biomarker of fibrosis progression (J Hepatol 2012) and of mortality (Gastroenterology 2011).

Aim:
Estimate the impact of SVR on the 10-year survival of fibrosis (SOFT) using repeated centralized interpretable FT and liver stiffness measurements (LSM) by FibroScan.

Methods:
In a prospective CHC cohort, the date of entry was the date of first FT. The main endpoint was a significant decrease of fibrosis, defined as FT decrease of at least 0.20, equivalent to 1 METAVIR stage. SOFT was estimated with the Kaplan-Meier method. The impact of SVR was estimated by logrank test and by Cox model including fibrosis risk factors: Alcohol, BMI, HIV, duration of treatment and the fibrosis progression rate (FPR) from birth to first FT.

Results:
902 pts were included: mean age 49.9yr, women 41%, genotype 1 69%, Caucasian 71%, BMI >30kg/m2 5%, alcohol consumption >30g/d 5%, HIV coinfection 25%. Mean (range) number of FT was 4.1 (2-9), over 4.1yr (1-14), and 2.9 (2-5) LSM over 3.0yr (1-7). Baseline fibrosis was F2F3F4 METAVIR in 44.5% (401/902) including 151 (16.7%) F4, and an FPR of 0.33. SVR was obtained in 178 (19.7%) pts and PCR was still positive in 724 (80.3%) pts (non-SVR). The overall SOFT was 94% (95%CI 92-96%, 332 pts still at risk) and 82% (95%CI 76-88%; 48 at risk) at 5yrs and 10yrs respectively. A fibrosis decrease was observed in 54 pts, almost all of them (51/54;94%) were F2F3F4. In these 401 pts, SVR (n=102) vs non-SVR (n=299), the SOFT were not different at 5yrs (83%;73-93% vs 90%;85-95%) but significant at 10yrs (46%;27-64% vs 76%;66-86% P=0.01). The only factor associated with SOFT in univariate/multivariate analysis was the persistence of detectable HCV RNA (Hazard Ratio;95%CI;Pvalue) /(Risk Ratio/95%CI/Pvalue) = (0.52;0.29-0.94;0.02)/(0.46;0.25-0.84/0.01). HIV, BMI, alcohol consumption, gender, ethnicity, genotypes and previous FPR were not significantly associated. For LSM, followup was shorter and no difference was observed at 5yrs: survival of LSM>=7.1 55% in SVR vs 57% in non-SVR (P=0.60). One case of hepatocellular carcinoma and one cholangiocarcinoma occurred in pts still F4 and F3.

Conclusion:
In CHC pts who had previously developed significant fibrosis, viral cure was not associated with fibrosis regression in 46 % of cases, 10 years later. Careful follow-up should be done to detect liver cancer and anti-fibrotic drugs are needed.