Impact of SVR on Liver Decompensation and Hepatic Fibrosis Markers in HIV/HCV

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Background / Rationale

- Chronic HCV is a major cause of morbidity and mortality in HIV
  - Rates of liver decompensation and extra-hepatic manifestations (esp. fractures, heart disease) are higher in HIV/HCV-coinfected than HCV-monoinfected patients
- Long-term consequences of sustained virologic response (SVR) to HCV treatment remain unknown in HIV/HCV
  - Few data on impact of SVR on decompensation, death in HIV/HCV
  - Unclear if hepatic fibrosis regresses after SVR, esp. with cirrhosis
  - Unknown if fibrosis regression rates after SVR differ by HIV status

Specific Aims

- **Aim 1**: Evaluate rates of decompensation and death after SVR in coinfected and monoinfected persons treated with IFN-based therapy
  - Hypothesis: Risks of decompensation and death are lower in persons who achieve SVR, regardless of HIV status
- **Aim 2**: Compare changes in hepatic fibrosis markers over time by SVR status in coinfected and monoinfected patients
  - Hypothesis: After SVR, rates of hepatic fibrosis (by non-invasive markers) will be lower for: 1) coinfected persons, and 2) patients with cirrhosis, regardless of HIV status

Methods

- **Study Design and Data Source**: Cohort study using data from Veterans Aging Cohort Study (VACS) and VA Hepatitis C case registry.
- **Study Patients - Eligibility Criteria**:
  - **HIV/HCV**: 1) HIV+; 2) HCV RNA+; 3) infected with genotype 1, 2, or 3; 4) received ≥4 weeks of PEG-IFN between 2002-2011, 5) on ART, 6) HCV RNA measured ≥12 weeks after end of HCV therapy
  - **HCV**: 1) HCV RNA+; 2) infected with genotype 1, 2, or 3; 3) no HIV, 4) received ≥4 weeks of PEG-IFN between 2002-2008, 5) HCV RNA measured ≥12 weeks after end of therapy
  - Follow-up: 1) Began at end of HCV therapy
    2) Continued until hepatic decompensation, death, subsequent HCV treatment course, or 30 Sept 2012
- **Main Outcomes**: Hepatic decompensation, death, platelet counts, aspartate aminotransferase (AST)-to-platelet ratio index (APRI) scores

Methods

- **Data Collection**:
  - Baseline: demographic, clinical, laboratory data
  - Longitudinal: ALT, AST, platelets, hepatic decompensation ICD-9 diagnoses (previously validated against medical records)
    - SVR: undetectable HCV RNA ≥12 weeks after treatment end date
    - APRI scores calculated at 12-week intervals
- **Statistical Analysis**:
  - Determined incidence rates of decompensation, mortality
  - Cox regression: hazard ratios (HRs) of decompensation and death associated with SVR in coinfected and monoinfected
    - Results stratified by baseline cirrhosis status (APRI ≥2.0)
  - Mixed effect regression models: biomarker trajectories

Selection of HIV/HCV-Coinfected Patients

1,004 HIV/HCV Patients Prescribed PEG-IFN (2002-2011)

632 Excluded:
- **48** Missing HCV genotype
- **19** HCV genotype 4, 5, 6
- **9** <4 weeks PEG-IFN
- **7** >96 weeks PEG-IFN
- **246** Not on ART
- **312** No HCV RNA ≥12 weeks after end of treatment

372 Eligible HIV/HCV Patients

Selection of HCV-Monoinfected Patients

23,810 HCV-Monoinfected Patients Prescribed PEG-IFN (2002-2008)

11,743 Excluded:
- **2,334** Missing HCV genotype
- **239** HCV genotype 4, 5, 6
- **66** <4 weeks PEG-IFN
- **219** >96 weeks PEG-IFN
- **8,501** No HCV RNA ≥12 weeks after end of treatment

12,067 Eligible HCV Patients

Characteristics and Outcomes, by SVR Status

HIV/HCV-Coinfected

Characteristics	No SVR (n=198)	SVR (n=174)
Mean age (SD)	51 (6.3)	52 (7.2)
Black race (%)	48%	31%
HCV genotype 1 (%)	82%	59%
2 (%)	11%	26%
3 (%)	7%	16%
APRI ≥2.0 at treatment (%)	8%	9%

Outcomes	Incidence Rate (events/1,000 p-yrs) No SVR	SVR	Adjusted HR,* SVR vs. No SVR (95% CI)
Hepatic decompensation	2.2 (2)	0.0 (0)	–‡
APRI ≥2.0 at treatment	29.1 (1)	0.0 (0)	–‡
APRI <2.0 at treatment	1.1 (1)	0.0 (0)	–‡
All-cause mortality	26.5 (43)	13.6 (14)	0.39 (0.21-0.72)
APRI ≥2.0 at treatment	20.4 (12)	12.5 (1)	–‡
APRI <2.0 at treatment	27.7 (31)	13.7 (13)	0.53 (0.27-1.04)

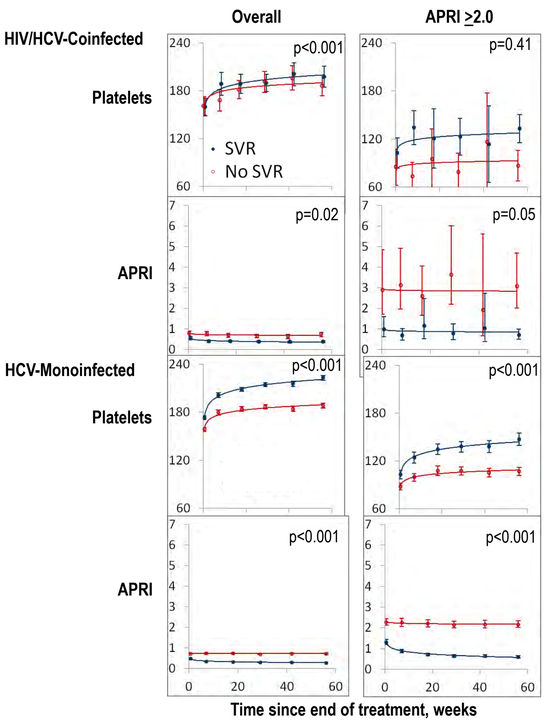
HCV-Monoinfected

Characteristics	No SVR (n=5,616)	SVR (n=6,451)
Mean age (SD)	52 (5.7)	52 (6.0)
Black race (%)	21%	11%
HCV genotype 1 (%)	82%	57%
2 (%)	9%	28%
3 (%)	9%	15%
APRI ≥2.0 at treatment (%)	14%	8%

Outcomes	Incidence Rate (events/1,000 p-yrs) No SVR	SVR	Adjusted HR,* SVR vs. No SVR (95% CI)
Hepatic decompensation	9.4	1.8	0.19 (0.14-0.17))
APRI ≥2.0 at treatment	36.6	7.3	0.21 (0.12-0.38)
APRI <2.0 at treatment	5.6	1.4	0.24 (0.15-0.37)
All-cause mortality	23.1	11.2	0.48 (0.41-0.56)
APRI ≥2.0 at treatment	58.3	17.2	0.29 (0.20-0.42)
APRI <2.0 at treatment	17.8	10.6	0.60 (0.50-0.71)

* Adjusted for age, race, sex, HCV genotype.
‡ Unable to determine adjusted HR because too few events in SVR group

Changes in Platelets and APRI After SVR, in HIV/HCV-Coinfected and HCV-Monoinfected



Conclusions

- SVR was associated with reduced risks of decompensation and death in HCV-monoinfected patients. No decompensations were observed in HIV/HCV patients who achieved SVR.
- Patients achieving SVR had greater improvements in liver fibrosis (based on APRI and platelets), regardless of HIV status.
- Future studies should compare decompensation events and changes in hepatic fibrosis after SVR with all-oral DAA therapies, by HIV status