Hepatic Decompensation in HIV/HBV/HCV Patients and the Impact of HBV Therapy

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Background

- Chronic hepatitis B virus (HBV) coinfection may be present in HIV/hepatitis C virus (HCV) patients
- No study has compared rates of hepatic decompensation in HIV/HBV/HCV triply-infected patients to those of HIV/HCV dually-infected individuals
  - Chronic HBV might exacerbate immune-mediated hepatic inflammation and fibrosis and increase the risk of decompensation among HIV/HCV patients
  - Alternatively, due to the reciprocal inhibitory effects of hepatitis viruses (i.e., replication of one hepatitis virus usually predominates over replication of the other in dually-infected persons), viral interference might lead to comparable decompensation rates between HIV/HBV/HCV and HIV/HCV patients.
- It also remains unclear if rates of hepatic decompensation in HIV/HBV/HCV triply-infected patients on anti-HBV nucleos(t)ide analogue therapy are similar to those of HIV/HCV dually-infected persons
- These analyses are important because they will:
  1. Clarify the impact of chronic HBV on end-stage liver disease progression in setting of HIV/HCV
  2. Determine the effectiveness of anti-HBV nucleos(t)ide analogue therapy among HIV/HBV/HCV patients

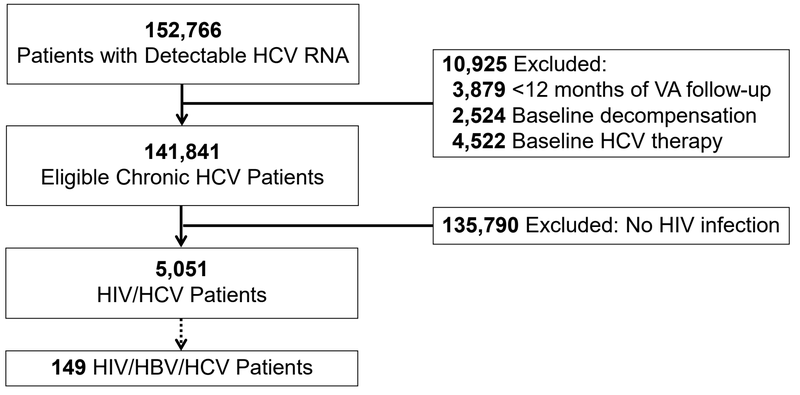
Specific Aims

- **Aim 1**: To compare the incidence rates of hepatic decompensation in HIV/HBV/HCV and HIV/HCV patients
  - **Hypothesis**: Rates of decompensation are higher in triply-infected persons
- **Aim 2**: To determine the risk of decompensation associated with anti-HBV nucleos(t)ide analogue-untreated and treated HIV/HBV/HCV infection
  - **Hypothesis**: Rates of decompensation will be increased among HIV/HBV/HCV patients who were not prescribed anti-HBV nucleos(t)ide analogue therapy

Methods

- **Study Design and Data Source**: Retrospective cohort study in the US Veterans Health Administration (VA) between 1 October 1 2005 and 28 February 2012
- **Study Patients:**
  - HIV/HBV/HCV patients had: 1) HIV, 2) HCV viremia, 3) chronic HBV (defined by two positive HBsAg results and/or two chronic HBV ICD-9 diagnoses recorded >6 months apart), and 4) at least 12 months of observation in the VA system
  - HIV/HCV patients had: 1) HIV, 2) HCV viremia, 3) at least 12 months in the VA , and 4) no positive HBsAg or chronic HBV diagnoses
  - Excluded: 1) baseline decompensation, or 2) baseline HCV therapy
  - Follow-up: 1) Began after 12 months in the VA system for both cohorts
    2) Continued until endpoint, death, HCV treatment, or 28 Feb 2012
- **Hepatic Decompensation**: Defined by 1 hospital ICD-9 diagnosis or ≥2 outpatient ICD-9 diagnoses of ascites, spontaneous bacteria peritonitis or variceal hemorrhage
- **Data Collected**: Comorbidities, medications, HIV/HCV lab results
- **Data Analysis:** Cox regression was used to:
  - Determine HR of decompensation in triply- versus dually-infected patients
  - Determine HRs of decompensation in anti-HBV nucleos(t)ide analogue-untreated and treated HIV/HBV/HCV patients compared to HIV/HCV patients

Selection of Patients



Baseline Cohort Characteristics

Characteristic	HIV/HBV/HCV (n=149)	HIV/HCV (n=4,902)
Mean age (years, SD)	52.2 (6.3)	52.7 (6.6)
Male sex (n, %)	146 (98.0)	4,790 (97.7)
Black race (no., %)	62 (41.6)	2,106 (43.0)
Hispanic (n, %)	32 (21.5)	286 (5.8)
Diabetes mellitus (n, %)	31 (20.8)	681 (13.9)
History of alcohol abuse (n, %)	46 (30.9)	1,027 (21.0)
HCV RNA ≥800,000 IU/mL (n, %)	96 (64.4)	3,529 (72.0)
HIV RNA <75 copies/mL (n, %)	60 (40.3)	1,657 (33.8)
CD4 <200 cells/mm^3(n, %)	15 (10.1)	492 (10.0)
On ART (n, %)	114 (76.5)	3,470 (70.8)

Hepatic Decompensation Events

Outcome	HIV/HBV/HCV (n=149)	HIV/HCV (n=4,902)
Total decompensation events (n, %)	16 (10.7)	230 (4.7)
Ascites	13 (81.3)	176 (76.5)
Spontaneous bacterial peritonitis	0 (0.0)	18 (7.8)
Variceal hemorrhage	6 (37.5)	68 (29.6)
Incidence rate of decompensation (events/1,000 p-years, IQR)	**24.1 (14.8 – 39.4)**	**10.8 (9.5 – 12.3)**

	Cohort	Adjusted HR (95% CI)*
Model #1	HIV/HCV	Ref.
	HIV/HBV/HCV	2.40 (1.44 – 3.99)
Model #2	HIV/HCV	Ref.
	HIV/HBV/HCV on HBV-active ART	1.09 (0.40 – 2.97)
	HIV/HBV/HCV not on HBV-active ART	2.48 (1.37 – 4.49

* Models adjusted for age, ethnicity, HCV RNA level, diabetes, and history of alcohol abuse.

Conclusions

- HIV/HBV/HCV patients had higher rates of decompensation than HIV/HCV patients
- Risk of decompensation was increased among triply-infected patients who did not receive an anti-HBV nucleos(t)ide analogue