Predicting the Risk of ESLD in HIV/HCV Patients for HCV Treatment Decisions

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Background / Rationale

- Despite the impact of HCV-related end-stage liver disease (ESLD) in HIV/HCV patients, no methods have been developed to predict the individual risk of ESLD within a specified time period by using clinical and laboratory characteristics
  - A prognostic model that quantifies the risk of ESLD in HIV/HCV could:
    - Prompt clinicians/patients to address modifiable risk factors for ESLD
    - Help determine which coinfected patients should be targeted for HCV therapy now and which could defer treatment until new more efficacious and tolerable direct-acting antiviral (DAA) regimens become available
    - Help weigh the benefits and risks of initiating interferon-based HCV treatment against the likelihood of progressing to ESLD over time, in settings where DAAs might not be readily available for HIV/HCV patients

Specific Aim

- **Specific Aim**: Evaluate the ability of clinical and laboratory variables to classify patients with HIV/HCV coinfection according to their risk of progression to ESLD

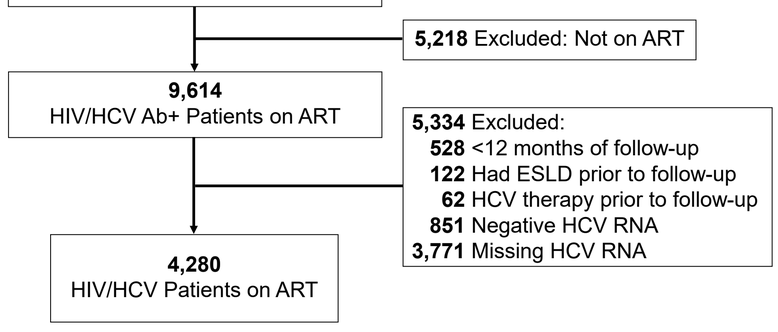
Methods

- **Study Design and Data Source**: Retrospective cohort study using data from Veterans Aging Cohort Study Virtual Cohort (VACS-VC) between 1997 and 2010
- **Study Patients:** Patients had: 1) HIV, 2) detectable HCV RNA, and 3) received ART for at least 12 months in VA system VACS-VC
  - Exclusions: 1) baseline ESLD, or 2) receipt of HCV therapy prior to follow-up
  - Follow-up: 1) Began after 12 months on ART in VA system
    2) Continued until ESLD, death, HCV treatment, or 31 Dec 2010
- **ESLD:** Defined by hepatic decompensation, hepatocellular carcinoma (HCC), or liver-related death, whichever occurred first
- **Baseline Predictors of ESLD**: Hemoglobin <10 g/dL, CD4 <200 cells/mm^3, HIV >400 copies/mL, diabetes, hepatitis B, non-black race, obesity, FIB-4 index
- **Statistical Analysis:**
  - Cox regression used to evaluate factors associated with ESLD
  - Fitted logistic regression models with outcomes of ESLD at 5 years
  - Area under receiver-operating characteristic curve (AUC) of models determined

Methods (cont'd.)

- Decision curve analysis evaluated usefulness of alternative models:
  - Plotted each model's predicted **net benefit** (relative harm of false-negative compared to false-positive classifications) on y-axis versus **threshold probability** (predicted risk of ESLD that prompts HCV therapy) on x-axis
  - Compared net benefit of a model with FIB-4 alone, alternative models with FIB-4 + other various clinical variables, initiating HCV treatment in all HIV/HCV patients, and treating none

Selection of HIV/HCV Patients



Predictors of ESLD

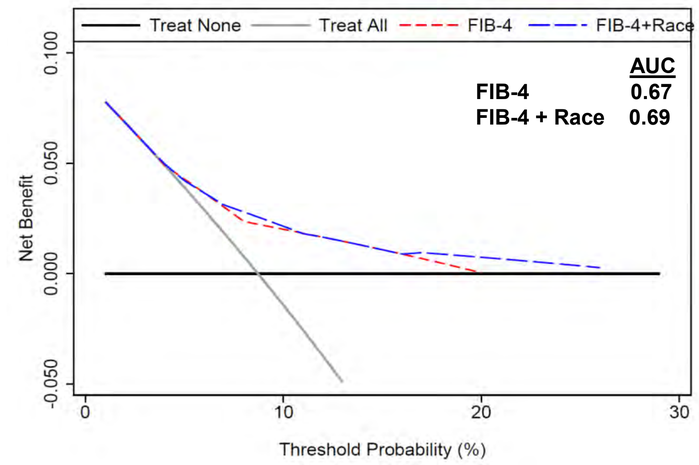
Baseline Predictor	n=4,280
Median age (years)	48
Non-black race (%)	34.9
Diabetes mellitus (DM, %)	7.4
Hemoglobin <10 g/dL (%)	2.5
CD4 count <200/mm^3 (%)	27.1
HIV RNA >400 c/mL (%)	63.4
HBsAg+ (%)	4.4
Obesity (%)	11.1
FIB-4 >3.25 (%)*	15.1

* FIB-4 determined by: (age*AST)/(platelets*(ALT)$^{1/2}$)

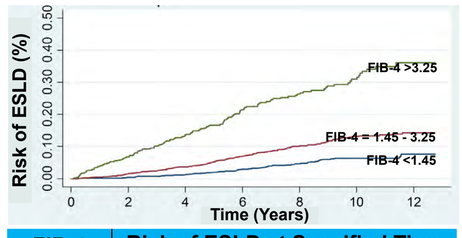
Incident ESLD Events

Outcome	n=4,280
ESLD (n, %)	373 (7.7)
Decompensation (n, %)	271 (72.7)
HCC (n, %)	74 (19.8)
Liver death (n, %)	110(29.5)
Median follow-up (years)	6.8

Decision Curve Analysis



Risk of ESLD, By FIB-4



FIB-4 Score	Risk of ESLD at Specified Time 1 Yr	3 Yrs	5 Yrs	7 Yrs	9 Yrs
<1.45	0.1%	1%	2%	4%	6%
1.45-3.25	0.6%	4%	5%	9%	12%
>3.25	4%	10%	17%	25%	29%

Conclusions

- FIB-4 has value in predicting risk of ESLD over time in HIV/HCV patients
- FIB-4 has prognostic value and might be useful for HCV treatment decisions