Conference on Retroviruses and Opportunistic Infections
March 3-6, 2014
Boston, MA, USA

Performance of the Framingham Risk Score in Hepatitis C-infected Persons

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Supported by the UCLA AIDS Institute and Center for AIDS Research (AI28697). This material is also the result of work supported with resources and the use of facilities at VA Pittsburgh Healthcare System, Pittsburgh, PA

Background

- Hepatitis C virus (HCV) infection may increase cardiovascular disease (CVD) risk, independent of traditional CVD risk factors.
- The Framingham Risk Score (FRS) is commonly used to predict 10-year coronary heart disease (CHD) risk, but its performance in HCV-infected persons is not well known.
- We hypothesized that the FRS underestimates CHD risk in persons infected with HCV.

Objective

- To evaluate the performance of the 10-year hard CHD FRS in HCV-monoinfected compared with uninfected controls.

Methods

Study Design and Subject Selection

- Retrospective cohort study utilizing the national Electronically Retrieved Cohort of HCV Infected Veterans (ERCHIVES), 2001-2009
  - HCV-infected and HCV-uninfected matched 1:1 by age, sex, race, year of HCV diagnosis in VA system
- Limited ERCHIVES dataset to male subjects ages 20-79 years without baseline CVD, diabetes, HIV, and chronic hepatitis B (eligible n= 316,514) and with calculable FRS (final n=232,816) for 10-year Hard CHD risk (using age, sex, systolic blood pressure, antihypertensive treatment status, smoking status, high-density lipoprotein [HDL-C] and total cholesterol level)
- Outcomes:
  1. Incident myocardial infarction (MI): 1 inpatient or 2 outpatient ICD-9 codes with date of diagnosis >6 months after entry
  2. Incident CHD: defined as MI, coronary artery bypass grafting (CABG), and/or percutaneous transluminal coronary angioplasty (PTCA) occurring >6 months after entry, by 1 inpatient or 2 outpatient ICD-9 codes
  3. CHD+Death (death from any cause)

Data Analysis

- Baseline characteristics and FRS were compared between the HCV-infected and uninfected groups by Kruskal-Wallis and Chi-squared tests
- Incident MI, CHD and CHD+Death event rates determined
- Follow-up time determined by time to first event or date of last contact
- Cox proportional hazards regression analysis used to calculate the hazard ratio (HR) for outcomes of interest by HCV status, adjusting for FRS (in FRS points, as a continuous variable), to determine if there was a persistent association between HCV infection and the outcome that was not captured by FRS
- Discrimination of MI risk by FRS determined using C-statistics, analyzed by HCV status and in the overall cohort by race/ethnicity

Results

Table 1: Baseline characteristics and predicted 10-year hard CHD risk by HCV status

Characteristic^	HCV-infected N=111,436	Uninfected N=121,380
Age (years)	52.7 (8.7)	52.4 (8.8)
Race/Ethnicity		
White	62,659 (56.2)	66,699 (55.0)
Black	30,039 (27.0)	33,723 (27.8)
Hispanic	6,365 (5.7)	7,376 (6.1)
Other/Unknown	12,373 (11.1)	13,582 (11.2)
BMI[X]	27.6 (5.3)	28.9 (5.6)
Systolic blood pressure (mmHg)	134 (15.9)	133 (15.2)
ALT (U/L)[α]	42 (26-72)	29 (21-42)
Chronic kidney disease		
Stage 0-2	101,005 (90.6)	110,124 (90.7)
Stage 3-5	10,431 (9.4)	11,256 (9.3)
History of drug abuse	29,552 (25.5)	15,007 (12.3)
History of alcohol abuse	30,161 (26.1)	20,593 (16.8)
Total cholesterol (mg/dL)	177 (153-205)	195 (170-224)
HDL-C (mg/dL)	43 (35-53)	43 (36-53)
LDL-C (mg/dL)[α]	105 (83-130)	119 (95-144)
Triglycerides (mg/dL)[X]	112 (78-166)	130 (88-199)
Smoking status		
Current	73,537 (67.0)	60,364 (49.7)
Former or never	37,899 (34.0)	61,016 (50.3)
On antihypertensive medication	65,067 (56.3)	74,289 (60.7)
On lipid lowering medication	18,313 (15.8)	36,994 (30.2)
Baseline predicted 10-year CHD risk by FRS, %	12 (6-16)	12 (6-20)
Mean follow-up (years)	3.9 (2.1)	4.1 (2.2)

^Data presented as n (%) or mean (SD) or median (IQR), Continuous variables compared by Kruskal-Wallis rank test, categorical variables by chi-square test. [X]Missing values in 1.4-1.9%, [α]Missing values in 5.7-8.8%

Table 2: Number of events during follow-up by HCV status

	HCV-infected	Uninfected
Incident MI	3118	3859
Incident CHD	3248	4023
Incident CHD+Death	17,859	12,345

Table 3: Event rates per 1000 person-years (95% CI) by HCV status

	HCV-infected	Uninfected
Incident MI	7.11 (6.87 – 7.37)	7.70 (7.46 – 7.94)
Incident CHD	7.41 (7.16 – 7.67)	8.03 (7.79 – 8.28)
Incident CHD+Death	40.8 (40.2 – 41.4)	24.6 (24.2 – 25.1)

Results

Table 4: Multivariable Cox proportional hazards model for incident CHD

Covariate	Hazard Ratio (95% CI)	P-value
HCV infection	0.94 (0.89 – 0.98)	<0.001
FRS	1.15 (1.14 – 1.16)	<0.001

Table 5: Multivariable Cox proportional hazards model for incident CHD +Death

Covariate	Hazard Ratio (95% CI)	P-value
HCV infection	1.68 (1.65 – 1.72)	<0.001
FRS	1.10 (1.09 – 1.10)	<0.001

Table 6: C-statistics for performance of FRS in MI risk discrimination by HCV status and race/ethnicity

	HCV	Uninfected	White	Black	Hispanic
C-statistic	0.62	0.61	0.61	0.61	0.62

Conclusions

- Higher Framingham risk score was associated with higher risk for incident CHD in this VA cohort by Cox regression analysis. HCV infection was associated with a slightly lower risk for incident CHD, which persisted after adjustment for FRS. However, risk of death was significantly higher in the HCV infected compared to the uninfected.
- By C-statistics, the FRS performed poorly at discriminating risk for MI in the cohort, in both HCV-infected and uninfected groups and across racial/ethnic groups.
- Poor discrimination of CHD risk by FRS in the cohort and the lack of an association between HCV infection and increased risk for incident CHD may be due to risk modifying variables over the follow-up period and competing risk of non-MI death over the follow-up period.
- Further analyses will be conducted to 1) adjust for competing risks for death in the cohort and 2) derive a new HCV-specific risk prediction score for CHD with improved risk discrimination.

Disclosures

K.W.C. and K.M.: none; D.B.: research support, Vertex Pharmaceuticals, Inc.; J.S.C.: grant support from Merck & Co., consultant for Viiv and Serono; A.A.B.: investigator-initiated grants from Merck & Co. and Pfizer.