21st Conference on Retroviruses and Opportunistic Infections, March 3-6, 2014, Boston, MA, USA

Hepatitis C (HCV) Viremia and the Risk of Acute Myocardial Infarction at Various Lipid Levels

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Background

- Hepatitis C virus (HCV) infection has been independently associated with a higher risk of coronary artery disease (CAD).
- The understanding of cardiovascular disease (CVD) risk in HCV infected populations is complicated by the differing prevalence of various CVD risk factors in HCV infected compared with uninfected persons and the poorly understood interaction of those factors.
- Serum lipid profile of HCV infected persons is substantially different than demographically similar HCV uninfected controls.
- Increasing severity of liver disease has been associated with progressively lower lipid levels, further complicating the association.
- Furthermore, it is unknown whether the lower serum lipid levels in HCV infected persons confers lower risk of CVD events in this population independent of other CVD risk factors.

Objective

To determine the association of lipid levels with the risk of acute myocardial infarction (AMI) in HCV infected and uninfected people.

Methods

We used ERCHIVES (Electronically Retrieved Cohort of HCV Infected Veterans), a well established national cohort of HCV infected Veterans and demographically matched HCV uninfected controls for our study.

The current study contains veterans identified from 2001-2008 from these sources. HCV infected subjects were identified based on a positive HCV antibody test.

HCV uninfected controls were identified based on a negative HCV antibody test in the same year as the positive test for the cases, and matched on age (5-year blocks), race, gender and geographical location.

Demographic and clinical information, including medical, psychiatric and substance use comorbidities were identified based on presence of at least one inpatient or two outpatient ICD-9 codes.

Laboratory data were retrieved from the Decision Support Service database and the Corporate Data Warehouse and included hemoglobin, white blood cell count, total cholesterol, triglycerides, high-density lipoprotein, low-density lipoprotein, alanine and aspartate aminotransferase, HCV antibody, and HCV RNA.

Pharmacy data were retrieved from the Pharmacy Benefits Management database and included drugs prescribed, dosage, number of refills and duration of prescription.

Presence of acute myocardial infarction (AMI) was defined by the presence of at least one inpatient or two outpatient codes for AMI.

We excluded subjects with HIV infection and diagnoses at baseline of CVD, chronic kidney disease stages 3-5, diabetes mellitus, hypertension, chronic obstructive pulmonary disease and smoking.

Since women comprised of less than 3% of the study population, they were excluded from analysis, as were those subjects who received at least 4 weeks of treatment for HCV.

From the remaining subjects, we retained those subjects who had complete clinical and laboratory data needed for our analysis.

Lipid levels were divided into groups based on the desirable levels set forth by the National Cholesterol Education Program, whereby the optimal or the desirable level was used as the comparator group, except for high-density lipoprotein, for which the comparator group was low HDL.

Baseline characteristics and lipid levels were compared between HCV infected and uninfected persons using chi-square test or t-test, as appropriate. We calculated the hazards ratios for a diagnosis of AMI by HCV infection status using Cox proportional hazards model. Assumptions of proportionality were tested using the Schoenfeld residuals.

Results

Within ERCHIVES, we identified 35,457 HCV infected and 45,299 HCV uninfected subjects who met the criteria detailed in Methods section. (Table 1) HCV infected persons had a lower body mass index (BMI) compared with HCV uninfected (27 + 5 kg/m2 vs. 29 + 5 kg/m2, p<0.001), lower total cholesterol (TC), low density lipoprotein (LDL-c) and triglyceride (TG) levels. High-density lipoprotein (HDL-c) levels were similar in both groups .

Among the HCV infected persons, we determined the risk of AMI in 5,979 persons with HCV viremia with 167 persons without viremia.

Table 1: Baseline characteristics of study population by HCV status among participants with complete information on several baseline covariates*

	HCV positive N=35,457	HCV negative N=45,299	p-value
	Mean (SD) or n (%)	Mean (SD) or n (%)	
Age in years	51.4 (9.6)	51.3 (9.7)	0.01
Race			
White	55	55	0.07
Black	25	24	
Body mass index, kg/m^2	27 (5)	29 (5)	< 0.0001
Total cholesterol, mg/dL	182 (40)	199 (40)	< 0.0001
<200	69%	53%	< 0.0001
200-239	22%	32%	
>240	8%	15%	
LDL-c, mg/dL	110 (36)	122 (37)	< 0.0001
<100	42%	26%	< 0.0001
100-129	31%	33%	
130-159	18%	26%	
160-189	7%	12%	
>=190	2%	4%	
HDL-c, mg/dL	46 (15)	46 (14)	0.87
<40	37%	35%	< 0.0001
40-59	46%	50%	
>=60	17%	15%	
Triglycerides, mg/dL, log$_{10}$	4.71 (0.55)	4.85 (0.58)	< 0.0001
<150	72%	62%	< 0.0001
150-199	13%	16%	
200-499	14%	21%	
>=500	1%	1%	

Table 2: Hazard ratios of myocardial infarction by HCVRNA status with adjustment for confounders*

		HCV-RNA positive N=5,979		HCV RNA negative N=167	
	Category	HR (95% CI)	p-value	HR (95% CI)	p-value
Total cholesterol, mg/dL	Ref	1.00(.,.)		1.00(.,.)	
	200-239	1.02(0.91,1.14)	0.73	0.58(0.11,2.97)	0.51
	>240	1.22(1.06,1.40)	0.01	0.66(0.08,5.66)	0.70
LDL cholesterol, mg/dL	Ref	1.00(.,.)		1.00(.,.)	
	100-129	0.95(0.84,1.07)	0.40	5.85(0.67,51.48)	0.11
	130-159	1.01(0.89,1.16)	0.85	1.25(0.08,20.21)	0.87
	160-189	1.06(0.89,1.26)	0.52	4.12(0.25,67.30)	0.32
	>=190	1.64(1.30,2.07)	<0.01	13.36(0.81,220.16)	0.07
HDL cholesterol, mg/dL	Ref	1.00(.,.)		1.00(.,.)	
	40-59	0.73(0.65,0.81)	<0.01	0.29(0.06,1.43)	0.13
	>=60	0.63(0.53,0.74)	<0.01	0.00(0.00,.)	1.00
Triglycerides, mg/dL	Ref	1.00(.,.)		1.00(.,.)	
	150-199	1.25(1.09,1.43)	<0.01	2.09(0.39,11.01)	0.39
	200-499	1.28(1.12,1.45)	<0.01	0.92(0.17,5.03)	0.92
	>=500	1.43(0.96,2.13)	0.08	0.00(0.00 ,.)	1.00

Results

Figure 1: Association of lipids with MI by subgroups of BMI among HCV positive and negative individuals

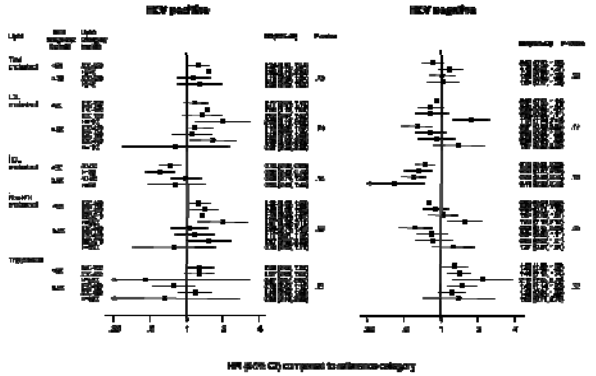
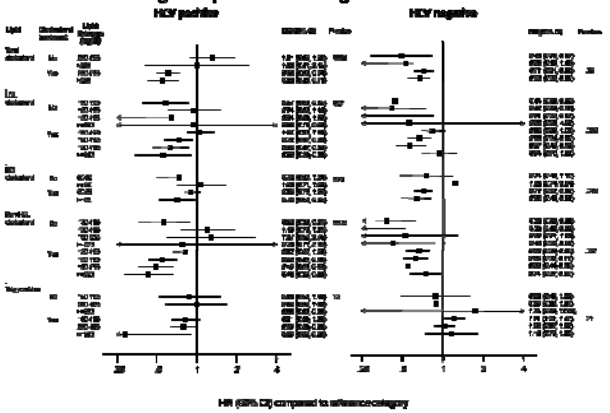


Figure 2: Association of lipids with MI by subgroups of lipid treatment among HCV positive and negative individuals



Conclusions

HCV viremia is associated with a higher risk of AMI at higher lipid levels compared with non-viremic persons and those with intermediate lipids levels.

At the highest levels within lipid categories, the risk of AMI is increased between 22-64%.

Treatment with lipid-lowering agents eliminated the higher risk of AMI.

Optimizing lipid levels and eliminating HCV viral replication are potential strategies to consider in lowering the risk of AMI in HCV infected persons.

Acknowledgement: This material is the result of work supported with resources and the use of facilities at VA Pittsburgh Healthcare System, Pittsburgh, PA