Depression and HIV Infection are Risk Factors for Heart Failure among Veterans

Jessica White[1], Chung-Chou Chang[2], Adeel Butt[3], Hilary Tindle[2], Maria Rodriguez-Barradas[4], David Rimland[5], David Leaf[6], Matthew Budoff[7], Amy Justice[8], Matthew Freiberg[2]

[1] University of Pittsburgh Graduate School of Public Health, Pittsburgh, PA; [2] University of Pittsburgh School of Medicine, Pittsburgh, PA; [3] Sheikh Khalifa Med City, Abu Dhabi, United Arab Emirates; [4] Baylor College of Medicine and Michael E. DeBakey VA Medical Center, Houston, TX; [5] Atlanta VA Medical Center; Emory University School of Medicine, Atlanta, GA; [6] VA Greater Los Angeles Health Care System, Los Angeles, CA; [7] University of California-Los Angeles, Los Angeles, CA; [8] VA Connecticut Health Care System; Yale University School of Medicine, New Haven, CT

Poster No. 726

BACKGROUND

HIV infection is associated with an increased risk of heart failure (HF). Depression is common among HIV infected (HIV+) and uninfected (HIV-) people and is also associated with incident HF. The high prevalence of depression among HIV+ adults may additionally increase the risk of HF.

Objective: To examine the association between depression and new-onset HF in a large cohort of HIV+ and HIV- Veterans.

METHODS

Cohort: Veterans Aging Cohort Study – Virtual Cohort (VACS-VC), a prospective study of HIV+ and their age-, sex-, race/ethnicity and clinical site-matched HIV- Veterans.

Participants: 81,427 Veterans (33% HIV+) from the VACS-VC without prevalent cardiovascular disease (CVD) at baseline.

Dependent variables: Veterans were followed from their first clinical encounter on or after 4/1/2003 until a HF event, death, or their last follow-up date (12/31/2009). Incident HF was determined if ICD-9 codes (428.xx, 429.3, 402.01, 402.11, 402.91, 425.xx) were present in at least 1 inpatient and/or 2 or more outpatient visits based on VA and Medicare record.

Independent variables:

HIV Status: Classified as HIV+ if they had at least 1 inpatient and/or 2 or more outpatient ICD-9 codes for HIV.

Depression: Depression was defined using the ICD-9 codes for major depressive disorder (MDD; ICD-9 codes 296.2x & 296.3x).

Covariates: All models were adjusted for age, sex, race/ethnicity, hypertension, diabetes, lipids, smoking, cocaine abuse, alcohol abuse, body mass index, HCV infection, renal disease (eGFR < 30 mL/min/1.73m^3), anemia (hemoglobin < 10 g/dL), statin use, atrial fibrillation, & atrial flutter. HIV-specific variables included baseline and recent CD4 cell count, HIV-1 RNA levels, and use of nucleoside reverse transcriptase inhibitors (NRTI), non-nucleoside reverse transcriptase inhibitors (NNRTI), & protease inhibitors (PI).

Statistical Analysis: Cox proportional hazards regression was used to model the association between HIV/MDD groups and incident HF, adjusting for covariates listed above.

Secondary analyses restricted the sample to include only HIV+ Veterans. These models were adjusted for all of the covariates above, plus the HIV-specific risk factors.

RESULTS

Table 1. Participant Characteristics by MDD Diagnosis & HIV Status

Characteristic	HIV-uninfected		HIV-infected	
	No MDD (n = 45, 728)	MDD (n = 8,791)	No MDD (n = 21,850)	MDD (n = 5,058)
Demographic Factors				
Age, years, mean (SD)	48.8 (9.5)	48.1 (7.4)	48.3 (9.7)	47.4 (7.9)
Male, %	97.5	95.6	97.7	95.3
Race / Ethnicity, %				
White	37.0	41.6	37.0	42.5
African American	48.0	46.8	48.5	45.9
Hispanic	7.5	9.2	6.9	8.2
Other	7.4	2.4	7.7	3.4
Baseline Cardiovascular Risk Factors, %				
Hypertension, Uncontrolled	32.4	29.0	25.7	23.6
Diabetes mellitus	20.0	23.1	13.3	16.1
Lipids, mg/dL				
LDL cholesterol ≥ 160	12.3	12.0	8.2	8.1
HDL cholesterol < 40	37.3	41.1	50.9	52.6
Triglycerides ≥ 150	37.4	42.2	46.9	49.1
Smoking				
Current	52.1	63.8	57.8	69.7
Past	16.5	13.4	13.7	11.0
Never	31.4	22.8	28.4	19.3
Cocaine abuse, dependence	5.5	16.3	8.5	23.3
Alcohol abuse, dependence	10.5	27.5	10.8	28.1
Body Mass Index ≥ 30 kg/m^2	38.7	38.6	13.7	16.6
HCV infection	13.9	24.0	32.7	43.2
eGFR < 30 mL/min/1.73 m^3	0.5	0.3	1.2	1.1
Hemoglobin < 10 g/dL	0.8	0.8	3.5	2.5
Statin use w/in 6 mos	9.4	11.6	6.4	6.8
Atrial fibrillation	0.96	0.81	0.82	0.65
Atrial flutter	0.26	0.38	0.25	0.22
HIV-specific Risk Factors, %				
CD4 cell count, < 200 mm^3	--	--	28.6	24.9
HIV-1 RNA, ≥ 500 copies/mL	--	--	55.1	56.5
NRTI use at baseline	--	--	48.3	49.6
NNRTI use at baseline	--	--	22.6	22.1
PI use at baseline	--	--	25.3	27.1

All comparisons were significantly different across the HIV/MDD groups (p < 0.01), except HIV-1 RNA level, NRTI use, and NNRTI use (p > 0.05)

Table 2. Rates and risks of incident HF by HIV/MDD group

	HIV-uninfected		HIV-infected	
	No MDD	MDD	No MDD	MDD
No. of HF events	1,339	319	774	234
Rates of HF per 10000 p-y (95% CI)	60.4 (57.3 - 63.8)	68.7 (61.6 - 76.7)	75.6 (70.5 - 81.1)	93.2 (82.0 - 106.0)
Risk of HF HR (95% CI)	**1.00 [Reference]**	**1.19 (1.05 - 1.35)**	**1.28 (1.16 - 1.41)**	**1.68 (1.45 - 1.95)**

Models were adjusted for age, sex, race/ethnicity, hypertension, diabetes, lipids, smoking, cocaine abuse, alcohol abuse, body mass index, HCV infection, eGFR, hemoglobin, statin use, atrial fibrillation, and atrial flutter

Additional results for Cox models

Risk factors significantly associated with HF included:

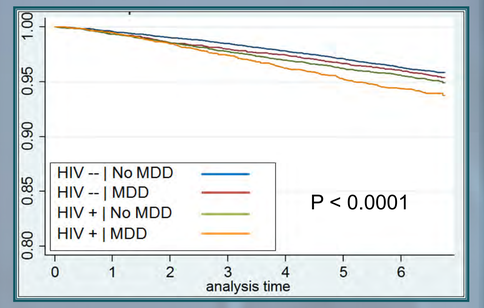
• Age	1.78 (1.70 - 1.86)
• Uncontrolled hypertension	1.94 (1.77 - 2.12)
• Diabetes	1.75 (1.61 - 1.91)
• Current smoking	1.42 (1.29 - 1.57)
• Cocaine abuse, dependence	1.27 (1.09 - 1.48)
• BMI ≥ 30	1.25 (1.14 - 1.36)
• HCV infection	1.30 (1.18 - 1.43)
• eGFR < 30	5.21 (4.31 - 6.30)
• Hemoglobin < 10	2.23 (1.75 - 2.85)
• Atrial fibrillation	2.15 (1.63 - 2.84)

Table 3. Cox proportional hazard regression models examining the association between MDD and incident HF among HIV+ Veterans

	HR of HF (95% CI)
Baseline HIV characteristics	1.30 (1.11 - 1.51)
Recent HIV characteristics	1.27 (1.08 - 1.48)

Models were adjusted for all variables from original model (see Table 2) as well as CD4 count, HIV-1 RNA levels, and NRTI, NNRTI, & PI use at baseline or at the most recent visit within 6 months.

Figure 1. Kaplan Meier survival analysis by MDD / HIV group



LIMITATIONS

- HF and depression were based on ICD-9 codes
- Clinical depression was measured at baseline
- Participants were predominantly men

CONCLUSIONS

- **Depression is associated with an increased risk for incident HF in both HIV+ and HIV- Veterans**
- **HIV+ Veterans with MDD is a vulnerable population at high risk for incident HF**
- **These findings reinforce current guidelines recommending screening for depression in the HIV+ population particularly those at risk for HF**

ACKNOWLEDGEMENTS

This work was supported by: NHLBI, T32 Cardiovascular Epidemiology Training Program HL083825-06, CVD – R01-HL095135; NIAAA, VACS – U10-AA013566; COMpAAAS – U24-AA020794, U01-AA020790