Depressive Disorders Predicts Incident Acute Myocardial Infarction in HIV+ Veterans: Veterans Aging Cohort Study

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BACKGROUND

- Incidence of acute myocardial infarction (AMI) is higher in HIV-infected patients than in uninfected patients. Because depressive disorders are independent risk factors for AMI in the general population and are highly prevalent in those with HIV infection, we examined the relationships between these psychiatric conditions and incident AMI in a large sample of HIV-infected patients.

Table 1. Baseline Characteristics of Participants Stratified by Depression Status

	No Depression Diagnosis (*N* = 21,131)	Any Depressive Disorder (*N* = 6,219)
Demographic Factors		
Age, years (mean ± SD)	48.4 ± 9.8	47.6 ± 7.9
Sex, male %	97.8	95.6
Race-ethnicity: White %	36.5	42.4
African American %	48.8	50.0
Hispanic %	6.8	8.2
Cardiovascular Risk Factors (%)		
Hypertension, uncontrolled	25.7	23.4
Diabetes	13.4	15.8
HDL cholesterol < 40 mg/dL	38.3	41.4
LDL cholesterol ≥ 160 mg/dL	5.9	6.1
Triglycerides ≥ 150 mg/dL	38.7	42.1
Statin use within 6 mo. of enrollment	6.4	7.0
Current smoking	53.0	66.5
Body mass index ≥ 30 kg/m^2	13.8	15.8
Other Important Covariates (%)		
Hepatitis C infection	32.3	43.9
eGFR < 30 mL/min/1.73m^2	1.5	1.3
Alcohol abuse or dependence	10.2	27.3
Cocaine abuse or dependence	7.9	22.7
Hemoglobin levels < 10 g/dL	3.4	2.4
HIV-Specific Factors (%)		
CD4 cell count < 200 mm^3	23.1	19.8
HIV-1 RNA levels < 500 copies/mL	37.4	35.4
ART regimen: NRTI plus PI	20.3	21.5
NRTI plus NNRTI	22.0	21.6
No ART	51.0	49.8

Are depressive disorders independent predictors of incident acute myocardial infarction among HIV-infected veterans?

METHODS

The Veterans Aging Cohort Study-Virtual Cohort (VACS-VC) is a cohort of HIV-infected and age, gender, race/ethnicity, and clinical site matched HIV-uninfected veterans who were identified from U.S. Department of Veterans Affairs (VA) administrative data in the fiscal years 1998-2003 using a modified existing algorithm.

The Ischemic Heart Disease Quality Enhancement Research Initiative (IHD-QUERI) is a VA research initiative designed to improve the quality of care and health outcomes of veterans with ischemic heart disease. As part of this initiative, data on all participants were reviewed from 2003 through 2009 to assess the system wide variations in acute coronary syndromes.

PARTICIPANTS: 27,350 HIV-infected veterans from the VACS-VC who were free of cardiovascular disease in October 2003.

INDEPENDENT VARIABLES: Depression cases were identified between 1998 and 2003 in the VA electronic medical record:
- Major depressive disorder (MDD; ICD-9 codes 296.2 or 296.3)
- Dysthymic disorder (ICD-9 code 300.4)
- Any depressive disorder (MDD or dysthymic disorder)

DEPENDENT VARIABLES: Incident AMI, determined by the IHD QUERI, was defined as:
- Discharge summary documentation and enzyme/ECG evidence of AMI (VA data),
- An inpatient ICD-9 code 410 (Medicare data),
- AMI (ICD-10 code 121) as underlying cause of death (death certificate data)

All patients were **followed for a median of 5.9 years** from their first clinic visit on or after April 1, 2003, to an AMI event, death, or the last follow-up date (December 31, 2009).

COVARIATES:
- **Demographic factors:** age, sex, race/ethnicity
- **CVD risk factors:** hypertension, diabetes, dyslipidemia, statin use within 6 months of enrollment, smoking, body mass index
- **Other important covariates:** hepatitis C infection, renal disease, alcohol and cocaine abuse/dependence, hemoglobin levels
- **HIV-specific factors:** CD4 cell counts, HIV-1 RNA levels, antiretroviral medication use

METHODS contd.

STATISTICAL ANALYSES:
- Incident AMI rates per 1000 person-years for the three depressive disorder variables (any depressive disorder, MDD, and dysthymic disorder)
- Three sets of Cox proportional hazards models for each depressive disorder variable. Each set was (1) adjusted for demographic factors, CVD risk factors, and other important covariates, and (2) further adjusted for HIV-specific factors.
- Kaplan-Meier survival curves to illustrate time from enrollment to first AMI event for participants with any depressive disorder versus no depressive disorder

RESULTS

- During the baseline period, **6,219 (23%) depressive disorder cases**, including **5,204 (19%) MDD cases** and **2,480 (9%) dysthymic disorder cases**, were identified.
- During the 5.9 years of follow-up, **367 (1.3%) incident AMI events** occurred.

Figure 1. Unadjusted Incident AMI Rates Per 1000 Person-Years by Depressive Disorder

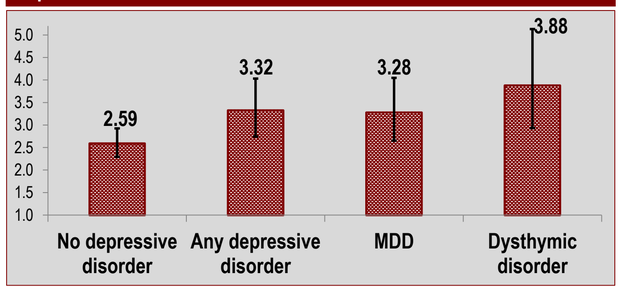
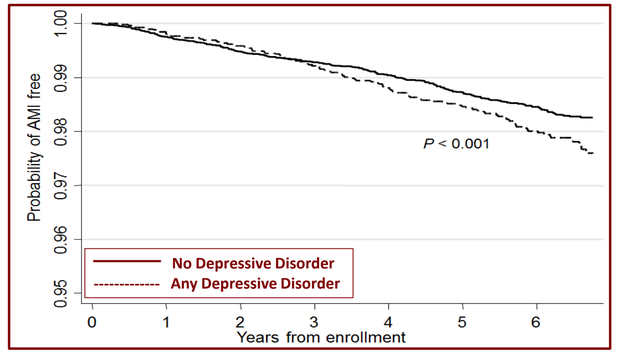


Table 2. Association of Depressive Disorders with Incident Acute Myocardial Infarction (separate models)

	Demographics, CVD Risk Factors, and Other Important Covariates Models	HIV- Specific Factors Models
	HR (95% CI)	HR (95% CI)
Any depressive disorder	1.31 (1.03-1.67)	1.31 (1.03-1.67)
MDD	1.27 (0.98-1.64)	1.28 (0.99-1.65)
Dysthymic disorder	1.46 (1.07-1.99)	1.47 (1.08-2.01)

Figure 2. Kaplan-Meier Survival Curves for Time to Event by Any Depressive Disorder



RESULTS contd.

- Incident AMI rates per 1000 person-years were higher among those with versus without **any depressive disorder (rate ratio 1.28, 95% CI: 1.01-1.62), MDD (rate ratio 1.24, 95% CI: 0.96-1.59)**, and **dysthymic disorder (rate ratio 1.46, 95% CI: 1.06-1.98)**, although the *HR* for MDD fell slightly below significance **(Figure 1)**.
- Cox proportional hazards models (adjusted for demographics, CVD risk factors, other important covariates, and HIV-specific factors) revealed that **any depressive disorder (*p*=.03; Figure 2)** and **dysthymic disorder (*p*=.01)** predicted incident AMI, while the HR for **MDD (*p*=.06)** fell just short of significance **(Table 2)**.

LIMITATIONS

- Using electronic medical record to identify cases with depressive disorders may have led to high specificity but low sensitivity as undiagnosed/unrecognized cases would not be properly classified.
- Due to our sample consisting primarily of male veterans, these results may not generalize to other populations with HIV infection.

CONCLUSION

- Our results suggest that depressive disorders are independent risk factors for AMI in the HIV-infected population.
  - Depressive disorders are associated with a 31% increased risk of AMI beyond that explained by known risk factors.
- Our findings provide preliminary support for future clinical trials to evaluate whether delivering evidence-based depression treatment may be a novel approach to managing the excess cardiovascular risk of HIV-infected patients with depression.