Elevated NT-pro-BNP levels predict mortality in HIV-infected women

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Background

Cardiovascular and pulmonary diseases are common comorbidities in HIV-infected individuals, but limited information exists on cardiovascular outcomes in HIV-infected women. Elevated N-terminal-pro-brain natriuretic peptide (NT-pro-BNP) is a marker of cardiac ventricular stress and provides a biomarker to assess the prevalence of cardiac disease, associated risk factors, and prognosis in patient cohorts with chronic HIV infection.

Objectives

- To determine if elevated NT-pro-BNP is associated with greater mortality in HIV-infected women.

Materials & Methods

Study design: Prospective cohort study

Subjects: Women's Interagency HIV Study (WIHS) participants. WIHS has 6 U.S. sites, is ongoing since 1994, follow up every 6 months, and has had additional enrollments in 2001-2002 and 2010-2012

Methods: NT-pro-BNP was measured from stored serum samples from a random sample of half the HIV-infected and matched (2:1) HIV-uninfected participants in WIHS at two time periods: early anti-retroviral therapy (ART) (10/11/94 to 7/17/97) and late ART (4/1/08 to 10/7/08). Covariates and time to death were extracted from WIHS data.

Analyses: The proportion of participants with NT-pro-BNP levels >75th percentile were compared by HIV status at each time point. Cox proportional hazards models were used to determine if an elevated NT-pro-BNP (>75th percentile) was associated with mortality independent of other covariates (age, race, body mass index, smoking status, alcohol use, illicit drug use, hepatitis C serostatus, hypertension, renal function, hemoglobin, history of AIDS, antiretroviral use, CD4 count, and viral load).

(Methods continued) Estimated survival curves for participants with average characteristics were created from the Cox proportional hazards models.

Results

- There were 387 HIV-uninfected and 936 HIV-infected and 448 HIV-uninfected and 1082 HIV-infected in the early and late ART periods, respectively (**Table 1**).
- NT-pro-BNP level was higher HIV-infected persons in both periods, but only significantly in the late period (26.6% vs. 21.2%, unadjusted p=0.03).
- An elevated NT-pro-BNP was associated with worse overall survival in HIV-infected persons during the early period (**Figure 1**).
- In HIV-uninfected persons during the early period, an elevated NT-pro-BNP was not associated with worse overall survival (**Figure 2**).
- During the late period, an elevated NT-pro-BNP was associated with worse overall survival in HIV-infected persons (**Figure 3**).

Table 1. Participant characteristics in the early and late HAART periods

	Early			Late		
	HIV-uninfected (N=387)	HIV-infected (N=936)	P-value	HIV-uninfected (N=448)	HIV-infected (N=1082)	P-value
Age (years)	34.8 (8.3)	36.8 (7.7)	<0.001	40.9 (9.7)	44.5 (8.2)	<0.001
African American	207 (53.5%)	541 (57.8%)	0.15	287 (64.1%)	614 (56.7%)	0.008
Hispanic	10 (2.6%)	39 (4.2%)	0.17	61 (13.6%)	156 (14.4%)	0.68
Body mass index(kg/m2)	28.5 (7.3)	27.0 (6.4)	<0.001	31.5 (8.7)	29.6 (7.5)	<0.001
Smoking Status, never	96 (24.8%)	260 (27.8%)	0.28	112 (25.0%)	360 (33.3%)	<0.001
Current smoker	225 (58.1%)	499 (53.3%)		220 (49.1%)	390 (36.0%)	
Former smoker	66 (17.1%)	177 (18.9%)		116 (25.9%)	332 (30.7%)	
Illicit drug use, ever	307 (79.3%)	707 (75.5%)	0.14	295 (65.8%)	516 (47.7%)	<0.001
Hepatitis C positive	111 (28.7%)	391 (41.8%)	<0.001	73 (16.3%)	265 (24.5%)	<0.001
History of AIDS		607 (64.9%)	n/a		478 (44.2%)	n/a
Current HAART		39 (4.2%)			849 (78.5%)	
CD4 counts: Current	1086 (388)	356 (281)	<0.001	1081 (394)	520 (290)	<0.001
HIV RNA detectable		842 (90.0%)	n/a		426 (39.4%)	n/a
NT-pro-BNP (above 3rd Quartile)	86 (22.2%)	245 (26.2%)	0.13	95 (21.2%)	288 (26.6%)	0.03

Values are the mean (standard deviation) or n (%).

Results

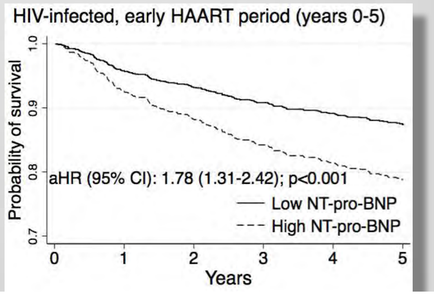


Figure 1: HIV-infected participants with an NT-pro-BNP>75th percentile (dash) had worse survival than those with an NT-pro-BNP≤75th percentile (solid) during the early HAART period. Deaths in low=87 and high=118. aHR = adjusted hazard ratio

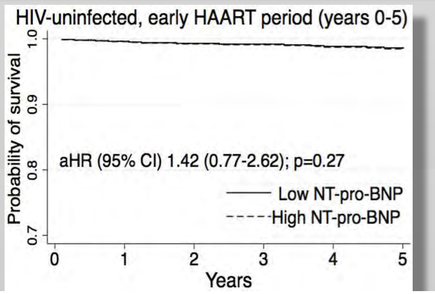


Figure 2: There was no difference in mortality in HIV-uninfected participants with either an NT-pro-BNP>75th percentile (dash) or and NT-pro-BNP≤75th percentile (solid) during the early HAART period. Deaths in low=8 and high=5. aHR = adjusted hazard ratio

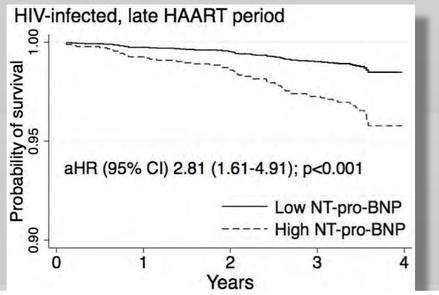


Figure 3: HIV-infected participants with an NT-pro-BNP>75th percentile (dash) had worse survival than those with an NT-pro-BNP≤75th percentile (solid) during the late HAART period. Deaths in low=23 and high=32. aHR = adjusted hazard ratio

Results

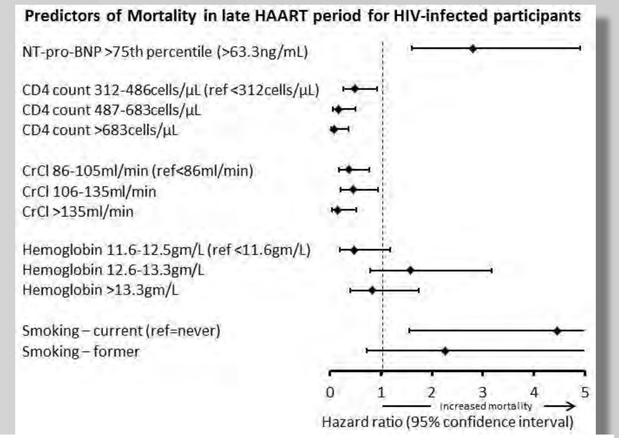


Figure 4: Cox proportional hazard model results for all-cause mortality in HIV-infected women from the WIHS cohort in the late HAART period.

- There were too few mortality events in HIV-uninfected persons during the late period to analyze the association with NT-pro-BNP level.
- Other factors associated with greater mortality in the late period HIV-infected persons were a low CD4 count, poor renal function, hemoglobin level, and actively smoking (**Figure 4**).

Conclusions

- NT-pro-BNP is a novel biomarker independently associated with greater mortality in HIV-infected women during both early and late ART periods.
- As NT-pro-BNP is often associated with cardiopulmonary dysfunction, the findings suggest that these conditions may contribute to adverse outcomes in this population.

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