Poster 700

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# HIV as a Risk Factor for Incident Pulmonary Hypertension

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## Background & Hypotheses

- Pulmonary hypertension (PH) is associated with increased mortality risk in veterans with HIV compared to veterans without HIV
- PH incidence based on echocardiographic measures of pulmonary artery systolic pressure (PASP) in both people with and without HIV remains unstudied
- *Hypothesis 1:* People living with HIV (PLWH) have higher PH incidence rates and risk versus individuals without HIV
- *Hypothesis 2*: PLWH with low CD4 cell count and/or high HIV viral load have greater PH risk than virally suppressed PLWH

## Methods

- 3,651 participants in the Veterans Aging Cohort Study (VACS) with echocardiographically measured PASP ≤35mmHg
- Baseline was date of participants' first echocardiogram on or after April 1, 2004; follow-up was through September 30, 2015
- PH incidence was defined as the presence of at least one subsequent echocardiogram with PASP >35mmHg
- Participants with a single echocardiogram or follow-up PASP measures <35mmHg were censored at date of death or September 30, 2015
- We estimated incidence rates of PH and disease progression (PASP increase >10mmHg) using Poisson regression stratified by HIV status as well as by CD4 cell count and HIV viral load
- We performed Cox proportional hazards regression to estimate risk of incident PH (and progression) in PLWH as a whole, by CD4 cell count, and by HIV viral load versus uninfected
- Multivariable adjusted models included age, sex, race/ethnicity, prevalent heart failure, COPD, BMI, eGFR, Hepatitis C virus infection, and FIB-4 as covariates.

## Results

- Median follow-up time: 3 years (Q1, Q3: 1, 7)
- When excluding individuals with prevalent HF and/or COPD, results attenuated but remained statistically significant, particularly in analyses with time-varying CD4 and HIV viral load (results not shown)
- African American race was associated with increased PH risk (HR [95% CI]: 1.33 [1.04, 1.70]) versus white race adjusting for HIV status.

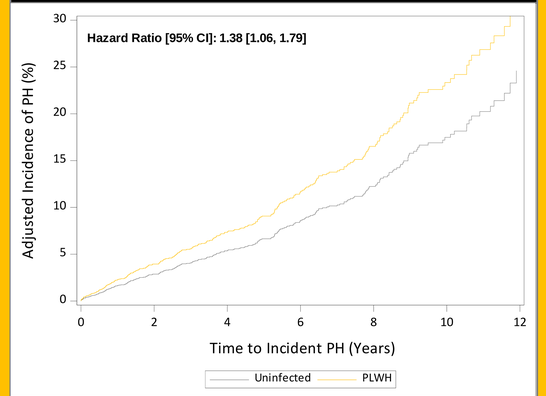
## Baseline Characteristics

| Characteristic | HIV Uninfected (N = 2476) | PLWH (N = 1175) |
|---|---|---|
| Age, years | | |
| Mean (SD) | 57.5 (9.7) | 57.3 (9.7) |
| Median | 58 | 57 |
| Male Sex | 97.1 | 97.8 |
| Race/Ethnicity | | |
| White | 40.9 | 41.9 |
| African American | 47.8 | 48.5 |
| Hispanic | 8.5 | 6.4 |
| Other | 2.8 | 3.2 |
| Prevalent HF | 2.2 | 2.1 |
| COPD | 31.7 | 31.9 |
| Hepatitis C Infection | | |
| Uninfected | 67.8 | 58.1 |
| Infected | 18.5 | 37.8 |
| Never Tested | 13.8 | 4.1 |
| FIB-4 | | |
| Mean (SD) | 1.7 (2.2) | 2.4 (3.5) |
| Median | 1.3 | 1.6 |
| eGFR, mL/min/1.73m$^2$ | | |
| Mean (SD) | 82.9 (30.2) | 81.8 (33.7) |
| Median | 82.3 | 81.3 |
| Body Mass Index, km/m$^2$ | | |
| Mean (SD) | 29.7 (6.4) | 26.1 (5.5) |
| Median | 29 | 25.3 |
| CD4 Cell Count, cells/mm$^3$ | | |
| Mean (SD) | -- | 451.8 (288.4) |
| Median | -- | 410 |
| HIV Viral Load, copies/mL | | |
| Mean (SD) | -- | 31083.2 (205544.7) |
| Median | -- | 50 |

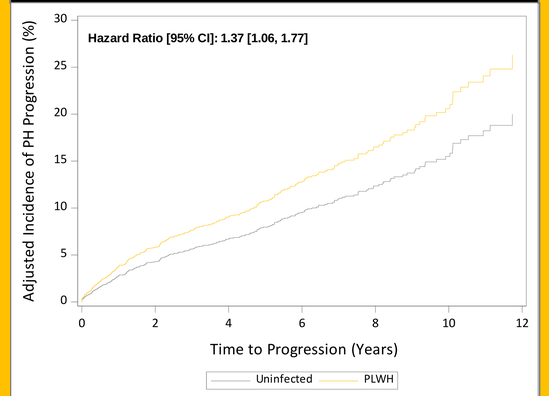
Abbreviayions: SD, standard deviation; HF, heart failure; COPD, chronic obstructive pulmonary disease; FIB-4, fibrosis 4 score; eGFR, estimated glomerular filtration rate.

All variables had complete data except Hepatitis C Infection (available on 1935 HIV uninfected and 979 PLWH), FIB-4 (available on 2381 HIV uninfected and 1050 PLWH), eGFR (available on 2452 HIV uninfected and 1169 PLWH), body mass index (available on 2469 HIV uninfected and 1173 PLWH), CD4 cell count (available on 960 PLWH), and HIV viral load (available on 965 PLWH).

## Adjusted PH Incidence by HIV Status




## Adjusted Progression by HIV Status




## Adjusted PH Incidence by HIV Status

| | | Incident PH (PASP > 35mmHg) | | | | Incident Progression (PASP Increase > 10mmHg) | | | |
|---|---|---|---|---|---|---|---|---|---|
| *Stratified by HIV Status and CD4 Cell Count* | | | | | | | | | |
| Group | N | PH Events | Rate/1000PY [95% CI] | Unadjusted PH Risk [95% CI] | Time-Varying CD4 Cell Count[a] | Progressions | Rate/1000PY [95% CI] | Unadjusted Risk [95% CI] | Time-Varying CD4 Cell Count[a] |
| HIV- | 2476 | 175 | 17.6 [15.2, 20.4] | 1 | 1 | 183 | 18.9 [16.3, 21.8] | 1 | 1 |
| HIV+, CD4≥500 | 358 | 29 | 22.3 [15.5, 32.1] | 1.42 [0.99, 2.02] | 0.98 [0.64, 1.51] | 29 | 22.9 [15.9, 33.0] | 1.35 [0.95, 1.93] | 1.01 [0.65, 1.56] |
| HIV+, 200≤CD4<500 | 422 | 29 | 18.4 [12.8, 26.4] | 1.16 [0.82, 1.66] | 1.34 [0.90, 2.00] | 35 | 22.8 [16.4, 31.8] | 1.22 [0.87, 1.70] | 1.49 [1.01, 2.19] |
| HIV+, CD4<200 | 180 | 19 | 33.3 [21.2, 52.2] | 1.84 [1.16, 2.92] | 2.60 [1.49, 4.53] | 20 | 36.9 [23.8, 57.2] | 1.81 [1.15, 2.86] | 2.17 [1.20, 3.91] |
| HIV+, Missing CD4[b] | 215 | 28 | 31.3 [21.6, 45.4] | --- | --- | 25 | 29.5 [19.9, 43.7] | --- | --- |
| *Stratified by HIV Status and Viral Load* | | | | | | | | | |
| Group | N | PH Events | Rate/1000PY [95% CI] | Unadjusted PH Risk [95% CI] | Time-Varying HIV Viral Load[a] | Progressions | Rate/1000PY [95% CI] | Unadjusted Risk [95% CI] | Time-Varying HIV Viral Load[a] |
| HIV- | 2476 | 175 | 17.6 [15.2, 20.4] | 1 | 1 | 183 | 18.9 [16.3, 21.8] | 1 | 1 |
| HIV+, VL<500 | 710 | 50 | 20.2 [15.3, 26.6] | 1.31 [0.97, 1.77] | 1.09 [0.78, 1.51] | 57 | 23.6 [18.2, 30.6] | 1.33 [1.01, 1.75] | 1.21 [0.88, 1.67] |
| HIV+, VL ≥500 | 255 | 26 | 26.9 [18.3, 39.5] | 1.50 [0.94, 2.40] | 2.33 [1.38, 3.92] | 26 | 27.9 [19.0, 41.0] | 1.46 [0.95, 2.24] | 1.79 [1.02, 3.16] |
| HIV+, Missing VL[b] | 210 | 29 | 32.3 [22.4, 46.4] | --- | --- | 26 | 30.8 [21.0, 45.3] | --- | --- |

*a* adjusted for age sex, race/ethnicity, prevalent heart failure, COPD, body mass index, eGFR, Hepatitis C virus, and FIB-4

*b* missing category used only for calculation of incidence rates. For models, missing CD4 cell counts and HIV viral loads were imputed

## Strengths & Limitations

*Strengths*

- Largest sample to date with echocardiographically measured PASP
- PLWH compared to demographically similar uninfected veterans

*Limitations*

- Assume that individuals without a second PASP measurement remained normal
- Sample is limited to veterans receiving care through the VHA and may not generalize to the general population or to women

## Conclusions

- HIV is independently associated with higher echocardiographic PH incidence after adjusting for risk factors
- Low CD4 cell count and high HIV viral load are associated with increased risk of incident PH and disease progression among PLWH
- Race may also contribute to differences in PH risk, but these associations require further study

## Acknowledgements

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