

The Association of Gender with Long-term Durability of ART and CD4 Count Rise

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Abstract

Background: Earlier studies have shown that women have not demonstrated the same benefit from ART as men. Previous data from Columbia Presbyterian Medical Center ID clinic suggest that women are less likely to be on ART when meeting DHHS criteria. It is not clear whether women have a virologic and CD4 response to ART similar to that of men.

Methods: Retrospective cohort study of all patients attending CPMC HIV clinic starting a first ART regimen after 1/1/97. Outcome measures were 1) having an HIV RNA viral load <400 copies/ml (UVL) within 24 weeks of starting ART, 2) time from first UVL till virologic failure defined as the first of two consecutive viral loads >400 copies/ml, and 3) slope of CD4 change after initiation of ART. Logistic regression was used to evaluate predictors of reaching UVL, and Kaplan-Meier analysis was used to evaluate time till virologic failure. The slope of CD4 change between groups was compared using a t-test after weighting by the individual slope variance.

Results: 229 patients were included, 35% were female. The reported HIV risk factors for women were heterosexual contact (84%), IDU (13%), and receipt of blood products (3%). The median baseline CD4 for women prior to starting ART was 133/mm³ compared to 63/mm³ for men (p=.09). The mean baseline log₁₀ viral load was 4.78 for women and 5.03 for men (p=.006). The median time from the first clinic visit to starting ART was 115 days for women compared to 61 days for men (p=.007). 7.5% of women failed to reach UVL compared to 19.5% men (OR 3.0, 95%CI 1.2-7.5). Baseline viral load, CD4, use of NNRTI versus PI and age were not related to reaching UVL. The significant factors for failing to reach UVL in the multivariate model were male gender (OR 4.6, 95%CI 1.5-13.7) and an HIV risk factor of IDU (OR 3.6, 95%CI 1.1-11.5). The proportion of women maintaining an UVL one year later was .79 (95%CI .69-.89), and three years later was .70 (95%CI .55-.86). These proportions were similar among men. The CD4 change for women after HAART was 122/mm³ per year vs. 113/mm³ per year for men (p=.13).

Conclusions: Women were started on ART with a similar CD4 as men, but were observed in the clinic for a longer time prior to initiating ART. Once starting ART, women were more likely than men to reach UVL. Men and women maintained a similar, durable virologic and CD4 response to ART.

Background

- Women have comprised 23% of persons with AIDS in New York City.
- A previous cross-sectional study at Columbia-Presbyterian suggested that women were less likely than men to be on ART when meeting DHHS criteria.
- Data are conflicting regarding gender differences of progression to AIDS in the absence of ART.
- Women tend to have lower HIV viral loads than men at similar stages of infection.
- Few studies have explored the long-term durability of ART in a clinic setting and how this response is associated with gender.

Results

- 7.5% of women failed to reach an undetectable viral load (UVL) compared to 19.5% of men, p=.02.
- Women were more likely than men to have a history of single NRTI exposure (p=.006).
- Women had a lower baseline viral load (p=.004) and a trend towards a higher CD4 count (p=.09).
- Women were less likely to have a history of an AIDS defining illness (p=.002) and started HAART at a younger age (p=.03).
- Significant factors associated with failing to reach UVL in the multivariate model were male gender (p=.01) and IDU as the reported HIV risk factor (p=.03). Trends were also seen for use of PI (p=.11) and history of single NRTI use (p=.09).

Table 1: Baseline Characteristics of Women and Men

| | Women (n=80) | Men (n=149) | p-value |
|-----------------------------------------------------|--------------|-------------|---------|
| HIV Risk factor | | | |
| IDU | 10 (13%) | 9 (6%) | ... |
| heterosexual contact | 64 (84%) | 85 (58%) | ... |
| MSM | na | 47 (32%) | ... |
| MSM/IDU | na | 2 (1%) | ... |
| Blood products | 2 (3%) | 3 (2%) | ... |
| Age at starting HAART | 37.7 | 40.8 | .026 |
| Previous AIDS defining illness | 27 (34%) | 82 (55%) | .002 |
| Median baseline CD4 count [IQ range] | 133 [41-260] | 63 [22-215] | .09* |
| Baseline log₁₀ HIV RNA viral load | 4.78 | 5.03 | .004 |
| Previous NRTI use | 14 (18%) | 9 (6%) | .006 |
| PI in regimen | 59 (74%) | 119 (80%) | .29 |
| Change in ART regimen in first 6 months | 17 (21%) | 35 (24%) | .69 |

*t-test comparing the log of baseline CD4 counts

Table 2: Univariate Analysis of Predictors for Failing to Reach an HIV viral load <400 copies/ml

| Predictor | Odds Ratio ¹ | 95% CI | p-value |
|------------------------------------------------|-------------------------|-----------|---------|
| Male gender | 3.0 | [1.2-7.5] | .02 |
| IDU as HIV risk factor | 2.9 | [1.0-8.2] | .05 |
| Age when starting HAART | 0.84 | [.21-3.4] | .81 |
| Previous AIDS defining illness | 1.5 | .[75-3.2] | .24 |
| Baseline CD4 count² | 0.92 | .[71-1.2] | .51 |
| Baseline HIV viral load³ | 1.2 | .[67-2.3] | .48 |
| Previous NRTI use | 1.6 | .[56-4.7] | .37 |
| PI in regimen | 2.5 | .[83-7.4] | .10 |
| Change in ART regimen in first 6 months | 0.90 | .[47-1.7] | .24 |

¹Modeled odds of failing to reach an undetectable viral load

²CD4 counts were modeled after log transformation

³HIV viral load was modeled after log₁₀ transformation

Table 3: Multivariate Analysis of Predictors for Failing to Reach an HIV viral load <400 copies/ml

| Risk Factor | Odds Ratio ¹ | 95% CI | p-value |
|-------------------------------|-------------------------|----------|---------|
| Male gender | 4.6 | [1.5-14] | .01 |
| IDU as HIV risk factor | 2.9 | [1.1-11] | .03 |
| Previous NRTI use | 1.6 | .[86-10] | .09 |
| PI in regimen | 2.5 | .[85-10] | .11 |

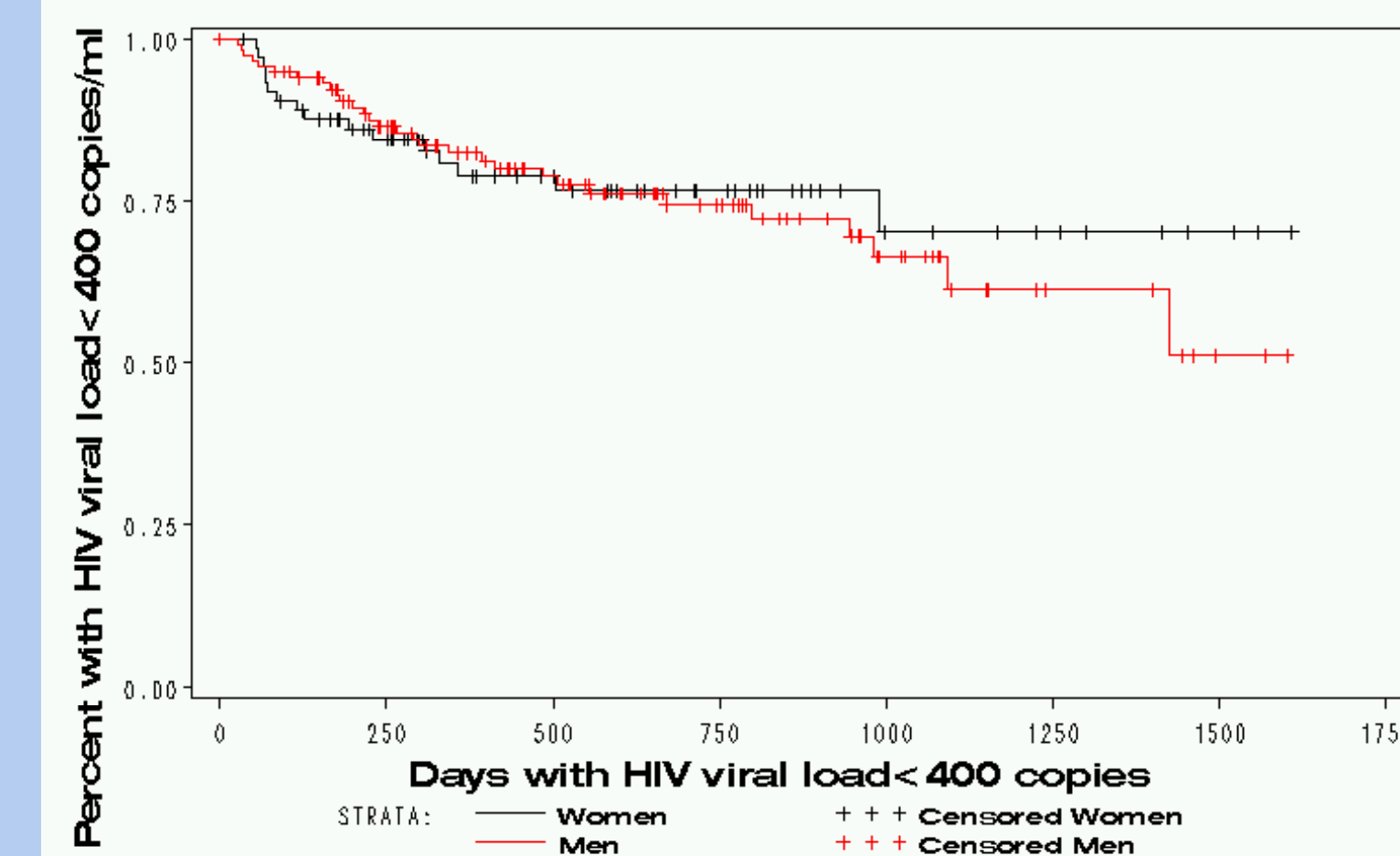
¹Models the odds of failing to reach an undetectable viral load

- Using a Kaplan-Meier analysis, the time to virologic failure once reaching an UVL did not differ between men and women (log-rank, p=.73). See Figure 1.
- The proportion of women maintaining an UVL one year later was .79 (95%CI .69-.89) and three years later was .70 (95%CI .55-.86). The proportions for men were .82 (95%CI .75-.89) and .61(95%CI .46-.76).
- The CD4 count rise after starting ART was similar for women (122 cells/mm³/year) and men (113 cells/mm³/year), p=.13.
- The predictors of virologic failure found to be significant in a Cox Proportional Hazards model are shown in Table 4.

Table 4: Predictors of Virologic Failure

| Predictor | Hazard Ratio | P-value |
|---------------------------------------|--------------|---------|
| PI containing ART regimen | 3.9 | .02 |
| Baseline CD4 count¹ | .80 | .05 |
| Age | .97/year | .04 |

¹ CD4 counts were modeled after log transformation



Methods

- Retrospective cohort study of all patients beginning first ART regimen at Columbia-Presbyterian Medical Center after 1/1/97.
- History of single NRTI use allowed; prior use of PI, NNRTI or dual NRTI excluded. Eligible regimens were 2 NRTIs + PI, 2 NRTIs + NNRTI, and 2 NRTIs + abacavir.
- Baseline variables included date of first clinic visit, date of first HAART use, previous NRTI use, previous AIDS defining illness, date of birth, gender, CD4 count and viral load prior to HAART, and choice of initial regimen.
- Outcome variables included reaching an HIV viral load <400 copies/ml (UVL), time till the first of two consecutive viral loads >400 copies/ml (for those reaching UVL), and CD4 count rise over the first two years. Patients leaving the clinic after reaching UVL were treated as censored.
- Univariate and multivariate logistic regression models were used to assess predictors of failing to reach UVL.
- Kaplan-Meier and Cox Proportional Hazards models were used to assess predictors of virologic failure once reaching UVL.
- The slope of CD4 count change was calculated for those patients having at least 2 CD4 counts post HAART by a linear regression of CD4 onto time and weighting according to the individual variance. Only CD4 counts within the first 24 months of starting HAART were used. A t-test was used to compare between groups.

Conclusions

- Women were observed in the clinic for a longer period of time than men prior to beginning ART. This may be due to their lower viral loads, trend towards higher CD4 counts and less frequent history of AIDS defining illness.
- Once starting ART, women achieved an HIV viral load <400 copies more often than men. This association persisted after adjusting baseline CD4 count, baseline viral load and prior NRTI use.
- The CD4 count rise after starting ART was similar for women and men.
- Both women and men had a durable response to ART similar to what has been reported in major clinical trials.