# 688 CYSTATIN C AND ATHEROSCLEROSIS IMAGING MARKERS IN HIV INFECTED PATIENTS

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## BACKGROUND

- Reduced estimated glomerular filtration rate (eGFR) using serum creatinine (Cr) based estimates is associated with increased risk of cardiovascular disease (CVD) in HIV
- Cystatin C (CC) is a protein produced by all cells of the body that is freely filtered and not reabsorbed. It has been used as an alternative to Creatinine for eGFR calculations.
- 3 CKD-EPI Equations have been developed to estimate GFR using Cr, CC, and a combination of Cr and CC (Cr-CC)
- Compared to eGFR using only Cr, serum CC-based eGFR is more predictive of CVD in the general population. However, it is unclear how CC-based eGFR compares to Cr-based eGFR in predicting subclinical CVD in HIV-infected persons

## METHODS

**We conducted a cross-sectional analysis** of data pooled from 3 large cohorts of HIV+ patients (VACS, MACS, Hawaii Aging)

- We compared associations between **3 CKD-EPI eGFR equations** (Cr, CC, and Cr-CC) with **2 atherosclerosis imaging markers**
  1. Intima media thickness at the common carotid artery (CIMT)
  2. Coronary artery calcium scores (CAC)
- CIMT, CAC, and CC were centrally measured

**Multivariable regression analysis**

- eGFR and CIMT were analyzed as continuous variables
- CAC scores were analyzed in 2 ways
  1. Binary: detectable vs non-detectable calcification
  2. $Log_{10}$ scale of Agatston scores in persons with detectable CAC
- Statistical significance was defined as P<0.05

**Covariates:**

- **Demographic factors:** age, sex, race/ethnicity
- **CVD and renal disease risk factors:** hypertension, diabetes, dyslipidemia, smoking, body mass index, hepatitis C infection
- **HIV-specific factors:** CD4 cell counts, HIV-1 RNA levels, antiretroviral medication use

**Characteristics**

3 large cohorts of HIV+ patients (VACS, MACS, Hawaii Aging)

- 97% Male, 35% black
- Median Age 52.34 ( SD 6.98) years
- 562 had CIMT measurements
- 296 had CAC measured
- 6.1-6.9% had eGFR <60 mL/min/1.73m$^2$
- 32.8-51.6% had eGFR <90 mL/min/1.73m$^2$

## RESULTS

- Mean (SD) CIMT was 0.79 (0.15) mm
- **For each 10 mL/min/1.73m$^2$ decrease in eGFR**
  - **Cr-CC eGFR** was associated with an **8.3µm (95% CI, 0.6-16µm; P=0.035) higher CIMT**
  - **Cr eGFR** was associated with a **7.6µm (95%CI, 0.0-1.51µm; P=0.052) higher CIMT**
  - **CC eGFR** was associated with a **5.4µm (95% CI, -1.5-12.3µm; P=0.124) higher CIMT**

- Of the 296 with CAC measures, **145 (49%) had detectable CAC**, with a **mean (SD) $log_{10}$Agatston score of 1.85 (0.79)**
- **Each 10 mL/min/1.73m$^2$ lower CC-eGFR** was associated with higher $log_{10}$Agatston score of **0.0941 (95% CI 0.0151-0.173; P=0.022)**
  - Associations with other eGFR formulae did not reach significance
  - eGFR was not associated with detectable CAC

**Table 1: Correlations with CIMT (µm)**

| | CIMT Creatinine Model | | CIMT Cystatin C Model | | CIMT Cr-CC Model | |
|---|---|---|---|---|---|---|
| Characteristics | Beta | P-value | Beta | P-value | Beta | P-value |
| **eGFR (mL/min/1.73m$^2$)** | -0.76 | 0.052 | -0.54 | 0.124 | **-0.83** | **0.035** |
| **Age (years)** | **5.14** | **<0.001** | **5.16** | **<0.001** | **5.00** | **<0.001** |
| Race Black | 27.48 | 0.124 | 25.64 | 0.182 | 27.87 | 0.147 |
| Race Hispanic | 11.49 | 0.561 | 11.40 | 0.581 | 13.78 | 0.505 |
| Current Smoker | 6.39 | 0.666 | 3.22 | 0.842 | 4.45 | 0.782 |
| **BMI (kg/m$^2$)** | **4.13** | **0.004** | **3.73** | **0.013** | **3.79** | **0.012** |
| HDL (mg/dL) | -1.61 | 0.138 | -1.64 | 0.140 | -1.56 | 0.161 |
| LDL (mg/dL) | -1.06 | 0.303 | -1.21 | 0.253 | -1.12 | 0.290 |
| Triglycerides (mg/dL) | -0.29 | 0.139 | -0.32 | 0.109 | -0.32 | 0.113 |
| Total Cholesterol (mg/dL) | 1.67 | 0.103 | 1.89 | 0.073 | 1.80 | 0.087 |
| **Systolic BP (mmHg)** | **2.36** | **<0.001** | **2.97** | **<0.001** | **2.98** | **<0.001** |
| **Diastolic BP (mmHg)** | **-2.93** | **0.002** | **-3.26** | **0.002** | **-3.29** | **<0.001** |
| **Antiretroviral use** | 32.69 | 0.147 | **51.38** | **0.031** | 48.34 | 0.045 |
| **Diabetes** | **57.09** | **0.010** | **51.05** | **0.033** | **51.17** | **0.032** |
| CD4 count (cells/mm$^3$) | 0.00 | 0.995 | 0.01 | 0.637 | 0.01 | 0.625 |
| **HIV-1 RNA (log copies)** | **29.95** | **<0.001** | **30.05** | **0.002** | **30.86** | **<0.001** |
| HCV Seropositive | 17.09 | 0.427 | 13.54 | 0.554 | 13.44 | 0.554 |

**Table 2: Correlations with CAC ($log_{10}$ Agatston)**

| | CAC Creatinine Model | | CAC Cystatin C Model | | CAC Cr-CC Model | |
|---|---|---|---|---|---|---|
| Characteristics | Beta | P-value | Beta | P-value | Beta | P-value |
| **eGFR (mL/min/1.73m$^2$)** | 3.29 | 0.449 | **-9.41** | **0.022** | -3.72 | 0.422 |
| **Age (years)** | **34.23** | **0.004** | **20.63** | **0.083** | **26.44** | **0.032** |
| Race Black | 215.01 | 0.319 | 302.47 | 0.173 | 290.95 | 0.207 |
| Race Hispanic | -430.99 | 0.213 | -536.48 | 0.125 | -455.77 | 0.201 |
| Current Smoker | -250.48 | 0.181 | -382.28 | 0.054 | -371.10 | 0.068 |
| BMI (kg/m$^2$) | 6.20 | 0.711 | 5.20 | 0.762 | 7.28 | 0.678 |
| HDL (mg/dL) | 4.64 | 0.601 | -0.52 | 0.954 | 1.05 | 0.911 |
| LDL (mg/dL) | 3.13 | 0.685 | -1.84 | 0.813 | -0.15 | 0.985 |
| Triglycerides (mg/dL) | 0.37 | 0.761 | -0.21 | 0.860 | 0.08 | 0.951 |
| TCholesterol (mg/dL) | -3.26 | 0.668 | 2.13 | 0.780 | 0.07 | 0.993 |
| Systolic BP (mmHg) | -9.46 | 0.181 | -11.80 | 0.103 | -12.51 | 0.092 |
| Diastolic BP (mmHg) | -5.25 | 0.658 | -1.33 | 0.912 | -0.49 | 0.968 |
| Antiretroviral use | 293.83 | 0.612 | -65.07 | 0.937 | -108.70 | 0.897 |
| Diabetes | 399.43 | 0.088 | 436.26 | 0.076 | 440.75 | 0.081 |
| CD4 count (cells/mm$^3$) | -0.44 | 0.138 | -0.29 | 0.336 | -0.34 | 0.262 |
| HIV-1 RNA (log copies) | 214.65 | 0.115 | 157.53 | 0.326 | 165.01 | 0.317 |
| HCV Seropositive | -92.04 | 0.617 | -223.90 | 0.256 | -96.33 | 0.619 |

## LIMITATIONS

- Patients were predominantly male
- Patients predominantly had eGFRs greater than 60 mL/min/1.73m$^2$, while pts most at risk for ASCVD may be those with lower eGFRs
- Cross-sectional analysis precludes assessment of causality
- Individual ART drug/regimen data not available for analysis
- Sample sizes for CAC analyses limited power to detect significant associations

## CONCLUSIONS

- Lower eGFR was significantly associated with higher CIMT when using the Cr-CC formula
- Lower eGFR was associated with higher CAC scores using the CC formula
- GFR estimating formulae incorporating cystatin C may identify HIV+ patients with subclinical CVD and for whom there is a greater need of aggressive CVD risk reduction

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