Biomarkers Influence Kidney Function Estimates More So Than Race Among Persons with HIV

830

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CURA PERSONALIS

translates as "care of the whole person," suggests individualized attention to the needs of others, distinct respect for unique circumstances and concerns, and an appropriate appreciation for singular gifts and insights.

BACKGROUND

- Kidney function estimation equations were revised in 2021 to exclude race, refuting earlier assumptions that creatinine (Cr) – a by-product of muscle metabolism – inherently differs by race.
- Cystatin C (CysC) is a biomarker produced by nucleated cells and can be used in conjunction with creatinine to estimate kidney function.
- We sought to understand the effects of different estimating equations and biomarkers on Chronic Kidney Disease (CKD) stage estimates among persons with HIV (PWH).

METHODS

Cross-sectional single site U.S-based study from 2014-2016.

Measurements:

- Routine Cr measurements were completed at a commercial laboratory and abstracted from the electronic health record.
- CysC was measured in a certified laboratory by immunoassay standardized to the ERM®-DA471/IFCC reference.

Kidney Function Estimating Equations:

- The 2009 CKD-EPI-Cr and 2012 CKD-EPI-Cr-CysC (which include race), and 2021 CKD-EPI-Cr and 2021 CKD-EPI-Cr-CysC (which exclude race) estimating equations were applied to stage renal function.

Statistical Methods:

- Agreement was assessed using differences of proportions.
- Regression analyses evaluated factors associated with CKD stage.
- Breslow-Day test evaluated whether race served as an effect modifier.
- SAS® (Version 9.4 SAS Institute Inc., Cary, NC).

RESULTS

- Among 306 participants, the median age was 48.2 years, 28% were female, 61% were Black, 30% Caucasian, 4% Latinx, and 15% had HCV co-infection (Table 1).
- The median CD4+ count was 659/mm^3, 98% were on ART, and 75% had HIV VL < 20 c/mL.
- Multivariable linear regression identified age, the interaction between tobacco use and absolute CD4+ count, and the interaction between HCV co-infection and nadir CD4+ count as factors associated with kidney function using the 2021 CKD-EPI Cr equation (aOR=3.25, 95% CI: 1.24-8.58) adjusted for age, tobacco use, absolute CD4, HCV co-infection, and nadir CD4 (Table 2).
- Race was not an effect modifier based on our analyses.

Table 1. Characteristics of the Study Population at Enrollment

Variable	Study Population (N=306)
Age (years; SD)	48.2 ± 11.3
Sex at Birth [n (%)]	
Female	86 (28.1)
Male	220 (71.9)
Race [n (%)]	
Black	185 (60.5)
Caucasian	91 (29.7)
Asian	4 (1.3)
American-Indian	1 (0.3)
Undetermined/Other	26 (8.5)
HCV Co-infection	45 (15)
Absolute CD4 (cells/ul; SD)	659 ± 301
On antiretroviral therapy [n (%)]	
Yes	299 (97.7)
No	7 (2.3)
HIV viral load < 20 c/mL [n (%)]	228 (74.5)
Serum Creatinine (mg/dL)	1.25 ± 1.65
Serum Cystatin C (mg/dL)	0.90 ± 0.69

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RESULTS

Comparison of Equations *Including Race* (2009 CKD-EPI Cr vs 2012 CKD-EPI Cr-CysC)

- More individuals were categorized as having normal kidney function (Stage I) with the addition of CysC vs Cr alone (73% vs 55%, p<0.00001)
- Fewer individuals were classified in CKD stages III-V with the addition of CysC than Cr alone (8% vs 12%, p=0.14).

Comparison of Equations *Excluding Race* (2021 CKD-EPI Cr vs 2021 CKD-EPI Cr-CysC)

- More individuals were classified as normal kidney function with inclusion of CysC vs Cr alone (74% vs 49%, p=0. 0.00001)
- Fewer individuals were categorized as CKD III-V with inclusion of CysC than Cr alone (8% vs 13%, p=0.026).

Table 2. Distribution of Kidney Function Estimates based on Estimating Equations

Stage	Kidney Function Classification	2009 CKD-EPI Creatinine*	2012 CKD-EPI Creatinine-Cystatin C*	2021 CKD-EPI Creatinine$^\phi$	2021 CKD-EPI Creatinine-Cystatin C$^\phi$
1	Normal/High	167	224	151	226
2	Mild	103	56	113	55
3a	Moderate	19	11	24	10
3b	Moderate	9	7	8	7
4	Severe	0	1	2	1
5	End-Stage	8	7	8	7

Note: The 2021 CKD-EPI Creatinine equation is the current clinical standard

*Denotes equations including race

$^\phi$Denotes equations excluding race

Conclusions

Among PWH, the addition of CysC shifted estimates of kidney function towards normal to a greater extent, even when using equations that exclude race.

Strategic use of CysC based kidney function assessment may provide useful information to guide clinical decisions in certain patient populations.