

# Race-modified estimated glomerular filtration rate underestimates chronic kidney disease prevalence in Black patients undergoing partial and radical nephrectomy: Implications for surgical planning

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## Abstract

**Introduction:** In estimated glomerular filtration rate equations (eGFR), the race multiplier (RM) yields greater eGFR values and may assign less severe chronic kidney disease (CKD) stages to black individuals. When deciding on appropriateness for partial nephrectomy (PN), patients with CKD are often considered a relative or absolute indication. We hypothesize that the eGFR RM may have ramifications for patients being counseled for radical nephrectomy (RN) versus PN to manage their renal tumor.

**Methods:** We utilized prospective and retrospective, IRB-approved single-center databases to select patients who underwent PN or RN between 2016 and 2022. Demographics, preoperative risk factors, preoperative eGFR, and surgical management were collected. Descriptive statistics and two-tailed difference of proportion tests compared the percentage of patients with CKD who underwent nephrectomy.

**Results:** This cohort included 1137 patients who underwent RN or PN, including 74 (6.5%) Black patients and 93.5% ( $n = 1063$ ) non-Black patients. There was no statistically significant difference between the eGFR of Black and non-Black individuals using the Modification of Diet in Renal Disease equation ( $P = 0.24$ ) or Chronic Kidney Disease Epidemiology Collaboration 2009 (CKD-EPI 2009) ( $P = 0.45$ ); however, there was statistically significant difference in eGFR between sample populations when using CKD-EPI 2021 ( $P = 0.0055$ ). Of the Black patient cohort, 16.2% of patients reclassified to a worse CKD class using CKD-EPI 2021, including 9.5% of Black patients reclassified to CKD3a or worse, and 14.6% of all patients (Black and non-Black) reclassified to a different CKD class under the CKD-EPI 2021 equation.

**Conclusions:** There are quantitative differences in the evaluation of eGFR when utilizing different equations that may impact clinical considerations and health equity outcomes for nephrectomy across racial groups.

**Keywords:** Nephrectomy, partial nephrectomy, race, radical nephrectomy, renal cancer

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## INTRODUCTION

The kidney carries multiple responsibilities, including maintenance of acid-base balance, regulation of fluid and electrolytes, absorption of certain small molecules, and clearance of toxins and metabolic waste products. A broad assessment of renal function is often determined by calculating the rate of filtration of creatinine, known as the estimated glomerular filtration rate (eGFR). The American Urological Association (AUA) guidelines highlight the use of eGFR for precise staging of preoperative kidney disease in assessing renal functional and suitability of surgical intervention.<sup>[1]</sup> The role of eGFR may also expand to systemic therapies as well as provide a basis to determine candidacy for dialysis or renal transplantation.<sup>[2,3]</sup> eGFR influences multiple aspects of clinical decision-making for possible nephrectomy patients requiring a reliable standardized method of determining preoperative renal function.

Creatinine is the most widely utilized endogenous filtration marker and is routinely assessed by serum creatinine ( $S_{Cr}$ ) for assessment of eGFR.<sup>[4]</sup> Equations utilize age, sex, and self-reported race to model eGFR.<sup>[5-9]</sup> The role of race in the equation was developed due to early studies demonstrating that Black individuals possessed higher levels of creatinine than white patients.<sup>[10]</sup> More recently, race has been called into question for its ambiguous role in medicine and potential to bias the eGFR, subsequently affecting treatment.<sup>[11,12]</sup>

Multiple race-based equations have come into practice in calculating eGFR using  $S_{Cr}$ . The Modification of Diet in Renal Disease (MDRD) as well as the Chronic Kidney Disease Epidemiology Collaboration 2009 (CKD-EPI 2009) equations have been most commonly utilized.<sup>[8,9]</sup> CKD-EPI 2009 has shown the highest accuracy in calculating eGFR and has been the standard for preoperative assessment of renal tumors.<sup>[1,9,13,14]</sup> More recently, the National Kidney Foundation and the American Society of Nephrology developed CKD-EPI 2021 with the removal of the race multiplier (RM) for the purpose of eliminating bias of self-identified race in treatment algorithms.<sup>[7]</sup>

Studies have shown that removal of the RM may increase CKD prevalence among Black adults, and those already classified with CKD may be revised to more severe disease stages.<sup>[15]</sup> eGFR equations have previously been reviewed in a variety of medical settings and specialties, including in patients with myocardial infarction and heart failure.<sup>[16,17]</sup> More recently, as shown by Antony *et al.*, race-neutral eGFR calculators perform equivalently

to prior eGFR equations while mitigating racial bias in nephrectomy decision-making.<sup>[18]</sup> In eGFR equations, the RM yields greater eGFR values and may assign less severe CKD stages to Black individuals. When deciding on appropriateness for partial nephrectomy (PN), patients with CKD are often considered a relative or absolute indication. This study aims to evaluate the impact of the RM on eGFR and how that may influence subsequent clinical decision-making. We hypothesize that the eGFR RM may have potential ramifications for patients being counseled for radical nephrectomy (RN) versus PN to manage their renal tumor.

## METHODS

This study utilized prospective and retrospective, IRB-approved single-center databases to select patients who underwent nephrectomy between 2016 and 2022. Demographics, preoperative risk factors, and laboratory values including  $S_{Cr}$  were collected within 1 week of surgery during preadmission testing. eGFR was calculated utilizing  $S_{Cr}$  according to the following equations:

### 1. CKD-EPI 2009:

- $eGFR = 141 \times \min(S_{Cr}/\kappa, 1)^\alpha \times \max(S_{Cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$  (if female)  $\times 1.159$  (if Black)

where:

- $S_{Cr}$  = serum creatinine in mg/dL
- $\kappa = 0.7$  for females and  $0.9$  for males
- $\alpha = -0.329$  for females and  $-0.411$  for males
- Min indicates the minimum of  $S_{Cr}/\kappa$  or  $1$  and max indicates the maximum of  $S_{Cr}/\kappa$  or  $1$ .

### 2. CKD-EPI 2021:

- $eGFR = 142 \times \min(S_{Cr}/\kappa, 1)^\alpha \times \max(S_{Cr}/\kappa, 1)^{-1.200} \times 0.9938^{Age} \times 1.012$  (if female)

where:

- $S_{Cr}$  = standardized serum creatinine in mg/dL
- $\kappa = 0.7$  for females or  $0.9$  for males
- $\alpha = -0.241$  for females or  $-0.302$  for males
- $\min(S_{Cr}/\kappa, 1)$  is the minimum of  $S_{Cr}/\kappa$  or  $1.0$
- $\max(S_{Cr}/\kappa, 1)$  is the maximum of  $S_{Cr}/\kappa$  or  $1.0$
- Age (years).

### 3. MDRD equation:

- $eGFR \text{ (mL/min/1.73 m}^2\text{)} = 175 \times (S_{Cr})^{-1.154} \times (\text{Age})^{-0.203} \times (0.742 \text{ if female}) \times (1.212 \text{ if Black})$ .

Patients were assigned to CKD stages based on eGFR using KDIGO guidelines, with Stage 1, 2, 3a, 3b, 4, and 5 defined by eGFR  $\geq 90$ , 60–89, 45–59, 30–44, 15–29, and  $<15$  mL/min/1.73 m<sup>2</sup>, respectively.<sup>[13]</sup> Assignment of race categories was on the basis of self-report.

### Statistical analysis

Categorical variables were expressed as counts and percentages, and continuous variables were expressed as mean and standard deviation. Descriptive statistics and two-tailed difference of proportion tests were used to compare the percentage of patients with CKD who underwent nephrectomy. Two-sided  $P < 0.05$  were considered statistically significant. All data transformation, graphical representation, and statistical analyses were performed using R version 4.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

## RESULTS

### Study population

Over the period between 2016 and 2022, 1137 patients received either an RN or PN with complete laboratory data for specific comparisons. The cohort was 65.0% male, with a median age of 63 (IQR 55–71) as shown in Table 1. The most common procedure performed was a PN, of which 71.3% of patients underwent, followed by RN with 28.7% of patients. In this cohort, 56.2% were never smokers, and patients had comorbidities including 21.5% with DM, 63.9% with HTN, 8.9% with CVD, 2.1% with CHF, and 9.1% with COPD. The cohort included 6.5% ( $n = 74$ ) Black patients, and 93.5% ( $n = 1063$ ) non-Black patients.

### Evaluation of glomerular filtration rate equations

Black and non-Black patient eGFRs were compared using the classic MDRD equation as well as the CKD-EPI 2009 and CKD-EPI 2021 equations. There was no statistically significant difference between the eGFR of Black and non-Black individuals using the MDRD equation ( $P = 0.24$ ) or CKD-EPI 2009 ( $P = 0.45$ ) as shown in Table 2; however, there were found to be statistically significant differences in eGFR between the sample populations when using CKD-EPI 2021 ( $P = 0.0055$ ).

Assigned patient CKD categories were compared using the CKD-EPI 2009 and CKD-EPI 2021 equations [Table 3]. Of the Black patient cohort, 16.2% of patients were reclassified to a worse class of CKD using the new CKD-EPI 2021 equation, including 9.5% of Black patients reclassified to CKD3a or worse. The non-Black patient cohort included 14.5% of patients reclassified to a better class of CKD using the new CKD EPI 2021 equation, and 14.6% of all patients (Black and non-Black) were reclassified to a different CKD class under the CKD EPI 2021 equation. A visual summary of patient reclassifications can be seen in Figure 1.

## DISCUSSION

This study examined a large retrospective and prospective

**Table 1: Baseline characteristics of the patient cohort, including Black and non-Black patients**

	Participants by race		Total
	Black	Non-Black	
Total (n)	74	1063	1063
Age	62 (56–69)	63 (55–71)	63 (55–71)
Sex			
Female	33 (44.6)	365 (34.3)	398 (35.0)
Male	41 (55.4)	698 (65.7)	739 (65.0)
BMI	30.2 (6.8)	29.5 (6.0)	29.5 (6.1)
Smoking status			
Never	41 (55.4)	598 (56.3)	639 (56.2)
Former	25 (33.8)	351 (33.0)	376 (33.1)
Active	7 (9.5)	106 (10.0)	113 (9.9)
Other	1 (1.4)	8 (0.8)	9 (0.8)
Surgery			
Radical	22 (29.7)	304 (28.6)	326 (28.7)
Partial	52 (70.3)	759 (71.4)	811 (71.3)
Comorbidities			
DM	30 (40.5)	214 (20.1)	244 (21.5)
HTN	56 (75.7)	670 (63.0)	726 (63.9)
CVD	5 (6.8)	96 (9.0)	101 (8.9)
CHF	3 (4.1)	21 (2.0)	24 (2.1)
COPD	6 (8.1)	97 (9.1)	103 (9.1)

Data are expressed as number of patients (%) or median (IQR). BMI: Body mass index, IQR: Interquartile range, DM: Diabetes mellitus, HTN: Hypertension, CVD: Cardiovascular disease, CHF: Congestive heart failure, COPD: Chronic obstructive pulmonary disease

**Table 2: Comparison of estimate glomerular filtration rate equations between Black and non-Black patient cohorts evaluating difference in the mean using two-sided  $t$ -tests**

	eGFR (mL/min/1.73 m <sup>2</sup> ), mean±SD		P
	Black	Non-Black	
MDRD	79.9±28.3	76.0±23.0	0.24
CKD 2009	80.6±28.2	77.9±21.9	0.45
CKD 2021	73.3±25.7	82.0±22.1	0.0055

SD: Standard deviation, CKD: Chronic kidney disease, MDRD: Modification of diet in renal disease, eGFR: Estimate glomerular filtration rate

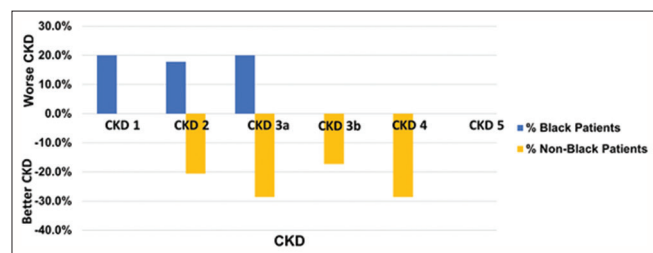
database of patients undergoing nephrectomy and compared multiple equations used in the evaluation of eGFR. For this study cohort, there was no statistically significant difference between Black and non-Black cohorts using the MDRD and CKD-EPI 2009 equations, both of which utilize an RM, but there was found to be statistically significant difference between groups when utilizing the newer CKD-EPI 2021 equation, which has dropped an RM from the equation. This difference may more appropriately reflect renal function when examining the patient groups' comorbidities, with DM present in 40.5% of Black patients compared to 20.1% of non-Black patients and HTN present in 75.7% of Black patients versus 63.1% of non-Black patients.

The mean eGFR of Black patients was found to be greater than non-Black patients utilizing both the CKD-EPI

**Table 3: CKD distributions for Black, non Black, and all patients using Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) 2009 and CKD-EPI 2021**

CKD-EPI 2009		CKD-EPI 2021						Percentage reclassified
Staging	n (%)	CKD 1	CKD 2	CKD 3a	CKD 3b	CKD 4	CKD 5	
<b>Black patients</b>								
CKD 1	30 (40.5)	25	5	0	0	0	0	20.0
CKD 2	28 (37.8)	0	23	5	0	0	0	17.8
CKD 3a	10 (13.5)	0	0	8	2	0	0	20.0
CKD 3b	2 (2.7)	0	0	0	2	0	0	0.0
CKD 4	0 (0.0)	0	0	0	0	0	0	0.0
CKD 5	4 (5.4)	0	0	0	0	0	4	0.0
Total, n (%)	74 (100.0)	25 (33.8)	28 (37.8)	13 (17.6)	4 (5.4)	0	4 (5.4)	16.20
<b>Non-Black patients</b>								
CKD 1	350 (32.9)	350	0	0	0	0	0	0.00
CKD 2	502 (47.2)	103	399	0	0	0	0	20.5
CKD 3a	133 (12.5)	0	38	95	0	0	0	28.6
CKD 3b	52 (4.9)	0	0	9	43	0	0	17.3
CKD 4	14 (1.3)	0	0	0	4	10	0	28.6
CKD 5	12 (1.1)	0	0	0	0	0	12	0.0
Total, n (%)	1063	453 (42.6)	437 (41.1)	104 (9.8)	47 (4.4)	10 (0.9)	12 (1.1)	14.5
<b>All patients</b>								
CKD 1	380 (33.4)	375	5	0	0	0	0	1.3
CKD 2	530 (46.6)	103	422	5	0	0	0	20.4
CKD 3a	143 (12.6)	0	38	103	2	0	0	28.0
CKD 3b	54 (4.7)	0	0	9	45	0	0	16.7
CKD 4	14 (1.2)	0	0	0	4	10	0	28.6
CKD 5	16 (1.4)	0	0	0	0	0	16	0.0
Total, n (%)	1137	478 (42.0)	465 (40.9)	117 (10.3)	51 (4.5)	10 (0.9)	16 (1.4)	13.5

CKD: Chronic kidney disease, EPI: Epidemiology collaboration, Patients highlighted pink have increased CKD staging from CKD-EPI 2009 with CKD-EPI 2021, and patients highlighted green have decreased CKD staging from CKD-EPI 2009 with CKD-EPI 2021



**Figure 1:** Differences in chronic kidney disease reclassifications of Black and non-Black patients based on glomerular filtration rate equations calculation using Chronic Kidney Disease Epidemiology Collaboration 2009 (CKD-EPI 2009) to CKD-EPI 2021. CKD: Chronic kidney disease

2009 and MDRD formulas; however, the mean eGFR of Black was calculated as less than the mean eGFR of the non-Black cohort when utilizing the CKD-EPI 2021 formula, which lacks an RM. This change can be seen in the reclassification of 16.2% of Black patients into worse CKD classes and reclassification of 14.5% of non-Black patients into better CKD classes. These results are similar to those found by Abdallah *et al.*, who recognized a shift to worse CKD stages in 27% of Black patients undergoing nephrectomy when utilizing the CKD-EPI 2021 equation from the CKD-EPI 2009 equation.<sup>[19]</sup>

The concept of removing the RM lowering eGFR for Black and increasing the eGFR for non-Black is not a novel concept and can be observed by studying the equations.

Buchkremer and Segerer graphically demonstrated the absolute and relative differences for Black and non-Black in eGFR between the 2009 and 2021 CKD equations, in which the most significant change is the removal of the RM.<sup>[20]</sup> We present in this study that these reclassifications in CKD can have significant implications in surgical planning. Patients who were reclassified into a worse CKD category should have a higher threshold to attempt a PN.

When comparing the CKD-EPI 2009, MDRD, and CKD-EPI 2021 equations, the removal of the RM suggested a relative decrease in the eGFR of Black compared to non-Black. These findings have potential ramifications for the use of eGFR in nephrectomy surgical planning based on the presence of CKD and may contribute to health-care inequalities. It should also be noted that changes in CKD of Black patients by alteration in eGFR equation and removal of an RM have multifaceted effects. Certain studies have demonstrated unintended consequences of attributing worse eGFR to Black patients such as in the setting of kidney donation, where worse eGFR may limit kidney donation in Black patients and possibly affect the ability of Black patients to receive a match due to common racial concordance between donors and recipients.<sup>[21,22]</sup> Non-Black patients also received substantial elevation in eGFR [Table 2] and were frequently reclassified into a different CKD class [Figure 1].

Limitations of this study include combined retrospective and prospective design. This limited some aspects of data collection and prediction of postoperative outcomes and mortality. Although this study included a sizable number of patients, when further dividing the cohort into procedure or racial groups the power of statistical comparisons was reduced. Our institution performs partial nephrectomies at a significantly higher volume than radical nephrectomies [Table 1], which could influence clinical conclusions. It is possible that with a larger cohort, and particularly a larger Black patient cohort as Black individuals constitute a minority of patients, stronger comparisons between groups could be drawn involving renal function, comorbidities, and outcomes.

Differences in comorbidities between patient groups may contribute to changes in kidney function and eGFR. The prevalence of these comorbidities such as DM have been found to differ across racial groups, have increased over time, and may further complicate evaluation of kidney function.<sup>[23]</sup> In addition, the evaluation of proteinuria was not conducted in this study, which may account for additional risk not estimated by eGFR.<sup>[24]</sup>

Although this study utilized  $S_{Cr}$  laboratory values on 24-h urine creatinine clearance were not obtained. Additional reference standards including iothalamate infusion could be considered for further evaluation of kidney filtration and function. Cystatin C has also been utilized as an alternative biomarker to creatinine for the assessment of renal function. It is important to clarify that equations purposed for eGFR only provide a convenient estimation of renal function, and although certain equations may broadly have an increased likelihood of matching a patient's actual GFR, each individual patient's renal function might be more accurately determined by a different equation or standard of evaluation.

Further, Black patients only comprised 6.5% ( $n = 74$ ) of this dataset of 1137 patients. This discrepancy from population levels may be attributable to individual and systemic barriers of minority groups, in addition to racial biases that may contribute to health disparities in clinical nephrectomy decision-making.<sup>[25]</sup> In addition, health-care inequities may have been exacerbated by the COVID-19 pandemic and subsequent logistical challenges.<sup>[26]</sup> A larger scale, more racially diverse population should be studied to further evaluate the race-specific effect of eGFR in clinical and surgical decision-making.

## CONCLUSIONS

Our study suggests that there are quantitative differences in

the evaluation of eGFR when utilizing different equations that may impact clinical considerations for nephrectomy across racial groups. Removal of the RM from eGFR equations creates a relative downward shift in mean eGFR of Black and upward shift of non-Black patients. These findings have potential ramifications for the use of eGFR in nephrectomy surgical planning based on the presence of CKD and may help address health disparities aiming toward increased rates of Black patients receiving PN over RN in the setting of lower eGFR.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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