

## Original Article

# Impact of race-based calculations of eGFR on the management of muscle invasive bladder cancer

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Received October 11, 2024; Accepted December 12, 2024; Epub December 15, 2024; Published December 30, 2024

**Abstract:** Purpose: The estimated glomerular filtration rate (eGFR) has historically been calculated with a race-coefficient multiplier (RCM); however, the RCM has been broadly criticized as inaccurate and a potential contributor to exacerbating disparities. We evaluated the impact of the RCM on eGFR and examined the 30-day post-cystectomy complications in a muscle-invasive bladder cancer cohort. Materials and methods: We retrospectively analyzed patients diagnosed with MIBC who underwent cystectomy in the ACS NSQIP database from 2006 to 2020 using CPT and ICD codes. The eGFR was computed using the Modification of Diet in Renal Diseases equation which has RCM = 1.212 for black patients. Using the race data field, patients were categorized into Black and non-Black. The eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup> was chosen for patient stratification because it represents a key clinical threshold in the classification of chronic kidney disease and influences various care decisions such as chemotherapy choice. Subsequently, we examined the 30-day post-cystectomy cardiovascular and pulmonary (CV&P) complications in these patients stratified by their eGFR using descriptive statistics and a multivariable logistic regression model. Results: The application of the RCM to estimate eGFR in the Black cohort increased the mean eGFR from 57.8 to 70.0 mL/min/1.73 m<sup>2</sup> (P = 0.001) which led to a 17.3% (45.6% vs 62.9%, P = 0.001) increase in the proportion of Black patients with eGFR ≥ 60 mL/min/1.73 m<sup>2</sup>. The rate of CV&P complications post-cystectomy among this group of 17.3% of patients in the Black cohort was 7.6% compared to a 4.3% complication rate among a non-Black cohort matched for similar eGFR for whom RCM was not applied (P = 0.06). Black patients in this RCM-dependent category of eGFR ≥ 60 mL/min/1.73 m<sup>2</sup> had higher adjusted odds of developing 30-day post cystectomy CV&P complications compared to eGFR-matched non-Black patients (OR = 2.2, 95% CI = 1.13-4.31, P = 0.02). Conclusion: In this study, we found that inclusion of RCM in the eGFR significantly increases the proportion of Black patients with eGFR ≥ 60. This RCM might also be associated with higher post-cystectomy CV&P complications; therefore, future studies are needed to evaluate the implications of race-based algorithms on outcomes.

**Keywords:** Estimated glomerular filtration rate (eGFR), race factors, urinary bladder neoplasms, outcomes, racial disparities

## Introduction

Estimated glomerular filtration rate (eGFR) derived from serum creatinine is widely utilized to estimate kidney function [1, 2]. Different thresholds of eGFR are used in MIBC management such as in cystectomy with neobladder and in determining eligibility for neoadjuvant chemotherapy. One of the clinically important eGFR cut-offs used is 60 mL/min/1.73 m<sup>2</sup> as

below this threshold, kidney function starts to decline disproportionately [3].

Until recently in clinical health practice, two equations have been historically used to calculate eGFR: the Modification of Diet in Renal Disease (MDRD) equation and the Chronic Kidney Disease Epidemiology Collaboration equation introduced in 1999 and 2009, respectively [1, 2]. These equations incorporate factors

such as age, sex, and race in calculating eGFR. Although recently cystatin-based and new creatinine-based eGFR equations have been proposed, this study focuses particularly on the historically used MDRD equation [4]. Notably, the MDRD equation includes a race coefficient multiplier (RCM) that increases eGFR by a factor of 1.212 for individuals identified as “Black” [1]. The RCM was included because, during the 1999 trial for the MDRD equation, Black race was incidentally found to be an independent predictor of higher urine creatinine excretion for both men and women [1].

There has been a growing concern that the inclusion of an RCM may exacerbate inequity for Black patients in clinical trials for anticancer drugs, kidney and liver transplant waiting periods, and Diabetes Mellitus management [5-8]. To address potential racial bias in clinical algorithms, in 2021 the National Kidney Foundation and the American Society of Nephrology established a task force aimed at exploring race-free options for eGFR calculations [9-11]. While the effects of removing RCM from eGFR calculations have been investigated in the field of kidney care, its impact on bladder cancer management has not been thoroughly studied [12]. Renal morbidity in a bladder cancer population that has been treated with radical cystectomy has been demonstrated in the literature [13]. The pathologic mechanism is multifactorial and associated with nephrotoxic treatments such as chemotherapy, advanced age, pre-existing kidney disease, which is prevalent in this population, and in some cases obstruction. Because cystectomy impacts the kidney function in MIBC patients, it is important to accurately estimate the presurgical kidney function in this group of MIBC patients [14].

This study specifically evaluated the impact of the RCM in eGFR calculations for a group of Black patients in which eGFR crosses a notable cut-off of 60 mL/min/1.73 m<sup>2</sup> solely due to the presence of race-coefficient (RCM) in the equation [15]. This cutoff is clinically relevant as it is widely used to categorize chronic kidney disease. Theoretically, the application of RCM to eGFR will increase the calculated GFR among Black patients thus increasing the number of such patients who cross the eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup>. However, if such calculations yield eGFRs that do not reflect actual renal

function, it leads to incorrect clinical decision making and, therefore, accentuating disparities. Using a national cohort of MIBC patients stratified by their eGFR around the cut-off of 60 mL/min/1.73 m<sup>2</sup>, we examined the 30-day post-cystectomy complications.

### Materials and methods

Using the American College of Surgeons National Surgical Quality Improvement Program (NSQIP®), we retrospectively analyzed patients aged ≥18 years who underwent cystectomy between 2006 and 2020 for MIBC.

#### *Inclusion and exclusion criteria*

All patients undergoing cystectomy who were postoperatively diagnosed with muscle-invasive bladder cancer were included. We used the Current Procedural Terminology (CPT) codes and International Classification of Diseases (ICD-9 and ICD-10) codes to identify such patients: for cystectomy we used (51550, 51570, 51580, 51555, 51565, 51590, 51575, 51596, 51585, 51595, 51597 and 50820). Subsequently, ICD-9 (188.0, 188.1, 188.2, 188.3, 188.4, 188.5, 188.6, 188.7, 188.8 and 188.9) and ICD-10 (C67.0, C67.1, C67.2, C67.3, C67.4, C67.5, C67.6, C67.8 and C67.9) were employed to identify the confirmed cases of post-operative diagnosis of MIBC. Patients with missing data on age, race, creatinine, and sex were excluded as these parameters are required for calculating the eGFR. Additionally, patients younger than 18 years were excluded, as muscle invasive bladder cancer is primarily an adult population disease.

#### *Exposure*

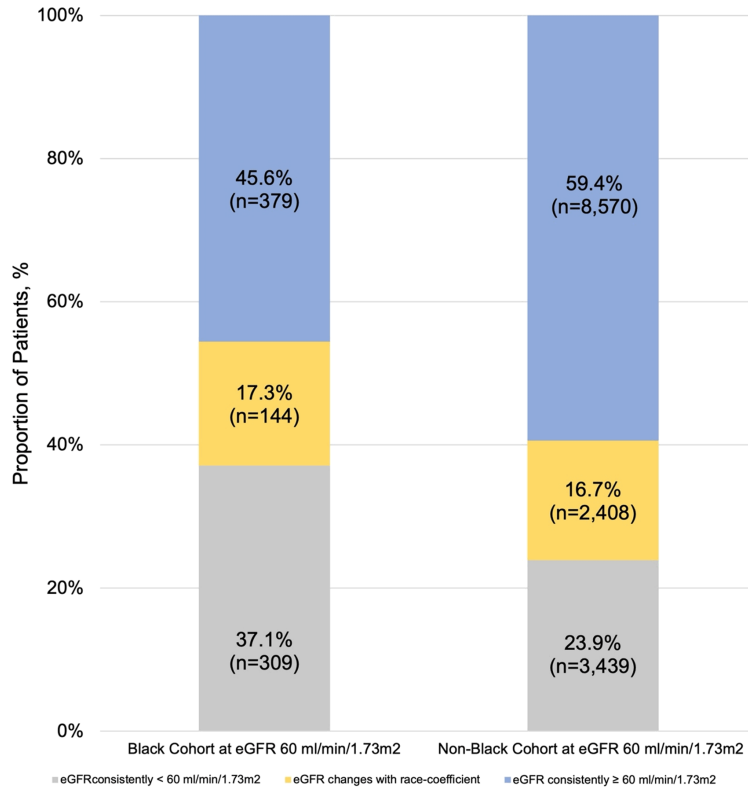
Creatinine was measured within the 30-day preoperative period. Our primary exposure for these patients was eGFR calculated using the Modification of Diet in Renal Diseases (MDRD) equation [1].

$$eGFR = 175 \times (SCr)^{-1.154} \times (age)^{-2.03} \times 0.742 \text{ [if female]} \times 1.212 \text{ [if Black]}$$

#### *Selection of controls*

Using the self-reported race variable, patients were categorized into Black and non-Black cohorts.

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**Figure 1.** Bar graphs show the percentage of Black and Non-Black cohorts (x-axis) diagnosed with muscle invasive bladder cancer (MIBC) and stratified by an estimated Glomerular Filtration Rate (eGFR) cut-off of 60 mL/min/1.73 m<sup>2</sup> into three different eGFR categories on y-axis. n represents the number of MIBC patients in each eGFR category.

Afterward, we utilized a two-step approach to stratify these patients for subgroup analysis. In the first step and for all Black patients, an RCM-inclusive eGFR (standard historical practice) was calculated; in the second step, an eGFR was calculated without the RCM. For the non-Black cohort, eGFR was initially calculated without applying the race coefficient, following standard historical practice. In the subsequent step, a race coefficient equivalent to that of Black patients (1.212) was applied to simulate eGFR as if they were Black. This two-step approach allowed us to categorize both Black and non-Black cohorts into three sub-categories based on a clinically meaningful eGFR threshold of 60 mL/min/1.73 m<sup>2</sup> (**Figure 1**) [16, 17].

### Stratification around an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup>

1. Those with an eGFR consistently ≥60 mL/min/1.73 m<sup>2</sup> regardless of the RCM in the equa-

tion. 2. Those with an eGFR consistently <60 mL/min/1.73 m<sup>2</sup> regardless of the RCM in the equation. 3. Those whose eGFR crosses the 60 mL/min/1.73 m<sup>2</sup> threshold based on the inclusion or exclusion of the RCM from the eGFR equation. For the Black cohort, if we calculate their eGFR as is used in standard historical practice, i.e., inclusive of RCM, then this subgroup of patients has an eGFR ≥60 mL/min/1.73 m<sup>2</sup>. However, if the RCM is removed, as has been advocated, their eGFR becomes <60 mL/min/1.73 m<sup>2</sup>. Similarly, for non-Black patients, if they had been treated like Black patients by assigning them an RCM, then this subgroup of non-Black patients would have an eGFR ≥60 mL/min/1.73 m<sup>2</sup>.

### Outcome

The primary outcome was 30-day post-cystectomy CV&P complications, as patients with chronic kidney disease (CKD) exhibit an elevated cardiovascular risk, manifesting as coronary artery disease, heart failure, arrhythmias, and sudden cardiac death [18]. We specifically observed cardiovascular and pulmonary (CV&P) complications, including either cardiac arrest, myocardial infarction, central nervous system/cardiocascular stroke, or pulmonary embolism.

The choice of 30-day post-op CV&P complications was made to evaluate an association between eGFR and its implications in a broader context of clinical management for MIBC patients, as complications within 30 days often have direct implications for patient recovery, healthcare resource utilization, and overall treatment effect [19]. Numerous studies have validated the use of 30-day outcomes as a meaningful and predictive timeframe [20]. It captures a significant portion of major complications without extending the monitoring period too far, which could dilute the focus on direct impacts based on presurgical evaluation.

## Statistical analysis

Using Stata version 17 B.E., Student's t-test, McNemar's test, and multivariable logistic regression models were employed for the analysis. In addition to examining the impact of the RCM on a clinically significant eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup>, we sought to examine the development of 30-day post-cystectomy CV&P complications in these patients stratified by their eGFR at a cut-off of 60 mL/min/1.73 m<sup>2</sup>. To test our hypothesis, we focused particularly on the patients whose eGFR crosses the 60 mL/min/1.73 m<sup>2</sup> threshold depending on the RCM in the eGFR equation, as shown in **Figure 1**. We hypothesized that these patients among the Black cohort had inaccurately calculated eGFR $\geq$ 60 mL/min/1.73 m<sup>2</sup> in contrast to their eGFR-matched non-Black counterparts whose eGFR was <60 mL/min/1.73 m<sup>2</sup>.

## Multivariable logistic regression

Therefore, we ran three multivariable logistic regression (MLR) models adjusted for age, sex, BMI, smoking status within the last year before cystectomy, and preoperative comorbidities. Preoperative comorbidities were defined as diabetes mellitus status, hypertension (defined as blood pressure  $\geq$ 140/90), history of chronic obstructive pulmonary disease (COPD), and any history of congestive heart failure. These regression models compared subgroups of the Black cohort to their eGFR-matched non-Black subgroups using an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup>. For instance, Black patients with an eGFR $\geq$ 60 mL/min/1.73 m<sup>2</sup> were compared to the non-Black patients with an eGFR $\geq$ 60 mL/min/1.73 m<sup>2</sup> in the first MLR model. Similarly, Black patients with an eGFR<60 mL/min/1.73 m<sup>2</sup> were compared to the non-Black patients with an eGFR<60 mL/min/1.73 m<sup>2</sup> in the second MLR model. Finally, in the third MLR model, Black patients whose eGFR crosses 60 mL/min/1.73 m<sup>2</sup> based on the inclusion or exclusion of the RCM in the eGFR equation were compared with the similar group among the non-Black cohort (simulated for RCM). This choice of comparison allowed us to measure the impact of racial factor (RCM) in estimating the kidney function and the management of MIBC patients.

## Results

### Demographics

Among the total of 15,249 participants, the Black cohort constituted 5.5% (832) of the sample population, while the non-Black cohort constituted 94.5%. The non-Black cohort included 97.3% Caucasians, 2.2% Asians, 0.1% Native Hawaiians or Pacific Islanders, and 0.4% American Indians or Alaska Natives. The Black and the non-Black cohorts were similar in BMI, history of COPD, and history of CHF but differed in serum creatinine (higher in Black cohort, difference = 0.2, *p*-value <0.01), history of hypertension, diabetes mellitus, and smoking status. Additionally, the Black cohort was younger (65.7 vs 68.9, *p*-value <0.01) than the non-Black cohort, with a higher proportion of women compared to non-Black women (*p*-value <0.01). The overall demographics of the patient cohort are shown in **Table 1**.

### Impact of RCM on mean eGFR

Including the RCM in the eGFR calculation for Black patients (as done in standard historical practice) led to a higher mean eGFR compared to the results excluding the RCM from the eGFR equation (70.7 versus 58.3 mL/min/1.73 m<sup>2</sup>, *p*-value <0.001).

### Impact of RCM on patient proportion $\geq$ 60 mL/min/1.73 m<sup>2</sup> eGFR

The inclusion of RCM in eGFR also increased the proportion of Black patients with an eGFR $\geq$ 60 mL/min/1.73 m<sup>2</sup> by 17.3% (*p*-value <0.001), as shown in **Figure 1**. To identify a matched group among the non-Black MIBC patient cohort, we identified patients with an eGFR<60 mL/min/1.73 m<sup>2</sup>, but who could have had an eGFR $\geq$ 60 mL/min/1.73 m<sup>2</sup> if their eGFR was also multiplied by the RCM. This RCM-dependent proportion of the non-Black cohort was 16.7% of the total non-Black cohort, as shown in **Figure 1**.

### Complications

Among the 17.3% of Black patients whose eGFR crossed 60 mL/min/1.73 m<sup>2</sup> solely due to the inclusion of the RCM in the eGFR equation, we found an increased rate of 30-day

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**Table 1.** Demographics of the patients in the Black and non-Black cohorts

	Black Cohort	Non-Black Cohort	p-value
N, %	832 (5.5%)	14,417 (94.5%)	<0.0001
Patient proportion at eGFR cut-off 60 mL/min/1.73 m <sup>2</sup>			
<60 mL/min/1.73 m <sup>2</sup>	309 (37.1%)	3,439 (23.9%)	<0.0001
≥60 mL/min/1.73 m <sup>2</sup>	379 (45.6%)	8,570 (59.4%)	<0.0001
eGFR changes with race-coefficient	144 (17.3%)	2,408 (16.7%)	<0.0001
Age [years], mean (SD)	65.7 (10.7)	68.9 (9.8)	<0.0001
BMI [kg/m <sup>2</sup> ], N (%)			0.017
>18-<25 kg/m <sup>2</sup> (ref)	252 (30.3%)	3,801 (26.4%)	
≤18 kg/m <sup>2</sup> (ref)	14 (1.7%)	163 (1.1%)	
≥25≤29 kg/m <sup>2</sup> (ref)	231 (27.8%)	4,539 (31.5%)	
≥29 kg/m <sup>2</sup> (ref)	335 (40.2%)	5,914 (41%)	
Sex			<0.001
Male	497 (59.7%)	11,148 (77.3%)	
Female	335 (40.3%)	3,269 (22.7%)	
Race			
Black	832 (5.5%)	-	
Caucasians	-	14,023 (97.3%)	
Asians	-	316 (2.2%)	
Native Hawaiians or Pacific Islanders	-	25 (0.1%)	
American Indians or Alaska Natives	-	53 (0.4%)	
Creatinine, mean [SD]	1.38 (1.03)	1.18 (0.61)	<0.0001
Diabetes Mellitus			<0.001
Yes	619 (74.4%)	11,686 (81.1%)	
No	213 (25.6%)	2,731 (18.9%)	
Smoker in the last year			<0.001
Yes	558 (67.1%)	11,175 (77.5%)	
No	274 (32.9%)	3,242 (22.5%)	
Hypertension, ≥140/90 mmHg			<0.001
Yes	256 (30.8%)	5,665 (39.3%)	
No	576 (69.2%)	8,752 (60.7%)	
History of Congestive Heart Failure			0.118
Yes	822 (98.8%)	14,313 (99.3%)	
No	10 (1.2%)	104 (0.7%)	
History of Chronic Obstructive Pulmonary Disease			0.021
Yes	785 (94.3%)	13,285 (92.2%)	
No	47 (5.7%)	1,132 (7.8%)	

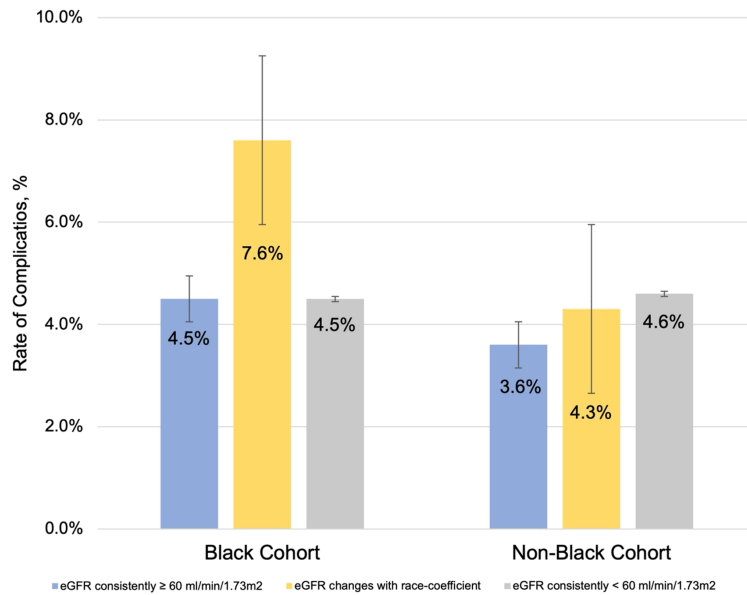
Key: eGFR was calculated using the Modification of Diet in Renal Diseases (MDRD) equation using the race-coefficient multiplier (RCM) and without the RCM (modified MDRD) as explained in the methods. Body Mass Index (BMI) was calculated using the formula: weight in kilograms divided by the square of height in meters (kg/m<sup>2</sup>). N, total patients within each cohort of black and non-black patients; eGFR, estimated glomerular filtration rate; SD, standard deviation; DM, Diabetes Mellitus; ref, reference value.

post-cystectomy CV&P complications uniquely observed in this group (**Figure 2**). The rate of observed CV&P complications in this subgroup was 7.6% versus 4.3% in an eGFR-matched non-Black cohort (P = 0.06). Based on a multi-variable logistic regression model, the odds of

developing CV&P complications in these 17.3% of Black patients were 2.2 times higher compared to the matched 16.7% of non-Black patients with similar eGFR (OR = 2.2, 95% CI = 1.13-4.31 and P = 0.02). For patients with consistently high or consistently low eGFR, no



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**Figure 2.** y-axis in the bar graphs show the rate of 30-day post-cystectomy cardiovascular and pulmonary (CV&P) complications in the muscle invasive bladder cancer cohort stratified by race and estimated Glomerular Filtration Rate (eGFR). On x-axis is the categories of Black and Non-Black cohorts stratified by eGFR at a cut-off of 60 mL/min/1.73 m<sup>2</sup>. Error bars indicate the standard errors. Rate of complications was calculated by dividing the number of patients developing CVP complications by all the patients in that eGFR category.

increased risk of 30-day post-cystectomy cardiovascular and pulmonary complications was observed between the Black and non-Black cohorts (Table 2).

Importantly, in our study, we found that race was not significantly associated with the development of CV&P complications overall, and rather only among the patients whose eGFR crossed the 60 mL/min/1.73 m<sup>2</sup> because of the inclusion of the RCM, suggesting that differences observed between the Black and non-Black cohorts for this subgroup were not due to race itself (Supplementary Table 1). We also ran a model (not shown) among Black patients only, in which we observed an increased risk of CV&P complications for patients whose eGFR crossed the 60 mL/min/1.73 m<sup>2</sup> cut-off with the race-coefficient compared to those whose eGFR remained  $< 60$  irrespective of the race coefficient (OR = 2.03, 95% CI = 0.8-4.7,  $p$ -value = 0.09). Although this was statistically non-significant due to the statistical power limitations of this study, it suggests increased complications in a group we hypothesized to have inappropriately higher eGFR $\geq 60$ .

## Discussion

Traditionally, eGFR calculations have included adjustments for race to account for potential differences in estimates of kidney function among different racial groups [1]. However, there is a growing recognition of potential racial bias inherent in these calculations [8]. For example, in the diagnosis of chronic kidney disease, it has been identified that the RCM falsely elevated eGFR, leading to delays in treatment for this disease [21]. This has sparked discussions in public health and clinical practice regarding the removal of race from clinical algorithms, such as eGFR equations [8]. In response, several academic medical centers transitioned to race-free calculations for eGFR in Black patients starting in 2021. This change was driven by concerns about disparities in access to anticancer medications excreted by the kidneys, clinical trial management, kidney transplantation, specialist care, and the broader misuse of race as a biological category [16, 22, 23].

In this study, our aim was to evaluate the estimates of kidney function in MIBC patients using an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup> among a Black patient population diagnosed with MIBC who underwent cystectomy as part of their management. We also aimed to examine an association between complications and clinically significant eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup> with special emphasis on the role of RCM in the equation. We specifically focused on the subgroup of Black patients whose eGFR crosses the threshold of 60 mL/min/1.73 m<sup>2</sup> by the choice of inclusion or exclusion of the RCM. Since RCM increases eGFR in Black patients for any given creatinine, we determined that the presence of RCM in eGFR also increases the Black patients' eligibility for treatment decisions requiring  $\geq 60$  mL/min/1.73 m<sup>2</sup>.

To better understand whether the prior paradigm of RCM-inclusive eGFR was potentially

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**Table 2.** Multivariable-adjusted logistic regression models to estimate 30-day post-cystectomy cardiovascular and pulmonary complications between different categories of Black and Non-Black cohorts, as determined by an estimated Glomerular Filtration Rate (eGFR) cut-off 60 mL/min/1.73 m<sup>2</sup>

	eGFR consistently ≥60 mL/min/1.73 m <sup>2</sup> irrespective of the race coefficient. Black (n = 379) Vs Non-Black (n = 8,570) <sup>a</sup>		eGFR consistently <60 mL/min/1.73 m <sup>2</sup> irrespective of the race-coefficient. Black (n = 309) Vs Non-Black (n = 3,439) <sup>b</sup>		eGFR changes with inclusion or removal of the race-coefficient. Black (n = 144) Vs Non-Black (n = 2408) <sup>c</sup>	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Non-Black Cohort (reference, [ref])	-	-	-	-	-	-
Black Cohort	1.37 (0.82-2.28)	0.22	1.05 (0.60-1.86)	0.87	2.2 (1.13-4.31)	0.02
Age (years)	1.03 (1.02-1.04)	<0.001	1.02 (0.99-1.03)	0.10	1.02 (1.00-1.05)	0.053
BMI (kg/m <sup>2</sup> )						
19-24 kg/m <sup>2</sup> (ref)	-	-	-	-	-	-
≤18 kg/m <sup>2</sup>	0.91 (0.28-2.98)	0.88	1.38 (0.32-6.02)	0.66	3.38 (0.69-16.64)	0.13
25-29 kg/m <sup>2</sup>	1.01 (0.73-1.40)	0.94	1.19 (0.76-1.88)	0.45	1.27 (0.73-2.24)	0.40
>29 kg/m <sup>2</sup>	1.52 (1.13-2.04)	0.005	1.88 (1.23-2.86)	0.003	1.7 (1.00-3.00)	0.050
Female [ref]	-	-	-	-	-	-
Male	1.23 (0.92-1.66)	0.16	1.35 (0.94-1.94)	0.10	0.97 (0.62-1.53)	0.90
Non-Smoker within the last 1 year [ref]	-	-	-	-	-	-
Current smoker within last 1 year	1.19 (0.90-1.56)	0.22	1.55 (1.04-2.33)	0.03	1.03 (0.62-1.73)	0.90
No DM/DM managed with diet [ref]	-	-	-	-	-	-
DM and currently on antidiabetic medications/Insulin	1.11 (0.96-1.30)	0.15	0.99 (0.80-1.23)	0.95	1.21 (0.95-1.54)	0.12
No hypertension requiring medication [ref]	-	-	-	-	-	-
Hypertension requiring medications	1.31 (1.02-1.68)	0.03	1.07 (0.73-1.56)	0.74	1.03 (0.67-1.59)	0.90
No History of severe COPD [ref]	-	-	-	-	-	-
History of severe COPD	1.41 (0.98-2.03)	0.07	1.26 (0.77-2.06)	0.35	2.58 (1.52-4.38)	<0.001
No History of CHF [ref]	-	-	-	-	-	-
History of CHF 30 days before surgery	4.63 (2.01-10.69)	<0.001	1.63 (0.57-4.64)	0.36	0.55 (0.07-4.26)	0.57

<sup>a</sup>Depicted in **Figure 1** as blue bars i.e., eGFR consistently ≥60 ml/min/1.73 m<sup>2</sup> irrespective of the race-coefficient in the eGFR equation. <sup>b</sup>Depicted in **Figure 1** as grey bars i.e., eGFR consistently <60 ml/min/1.73 m<sup>2</sup> irrespective of the race-coefficient in the eGFR equation. <sup>c</sup>Depicted in **Figure 1** as yellow bars i.e., eGFR in these patients changes with the inclusion or removal of race-coefficient (1.212) from the eGFR equation. Abbreviations/Key: 95% CI, 95% confidence interval; OR, odds ratio; COPD, chronic obstructive pulmonary disease; CHF, congestive heart failure; DM, diabetes mellitus; BMI, Body Mass Index = weight (kg)/height (m)<sup>2</sup>; eGFR, estimated glomerular filtration rate. All three a, b, and c multivariable-adjusted logistic regression models were adjusted for Age, BMI, Sex (male, female), Smoking Status within the last one year, Diabetes Mellitus Status, Hypertension (defined as ≥140/90 mmHg (systolic blood pressure/diastolic blood pressure)) requiring medications, history of severe chronic obstructive pulmonary disease, and history of congestive heart failure 30 days before surgery. ref indicates Reference value.

harmful to patients, we examined the development of 30-day post-cystectomy cardiovascular and pulmonary complications with the hypothesis that a potentially inaccurately elevated eGFR due to RCM might correlate with a higher risk of post-cystectomy complications, and thus potentially put these patients at higher risk of harm from inappropriate eligibility for certain treatments [19]. By examining a national database, we sought to document the advantages and disadvantages of including or excluding the race-coefficient in eGFR calculations.

Our findings demonstrated that the RCM-dependent  $eGFR \geq 60$  mL/min/1.73 m<sup>2</sup> subgroup of Black patients had a disproportionately higher incidence of CV&P complications at a 7.6% rate compared to a <5% rate of complications in all other categories of the Black and non-Black cohorts ( $p$ -value = 0.036) as defined by an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup> (Figure 2). This is a notable finding, as Black and non-Black patients with poorer renal function had fewer complications than this subgroup. This anomalous rate of 30-day post-cystectomy cardiovascular and pulmonary complications raises concerns about the clinical implications of using race as a factor in estimates of kidney functions.

To further examine the association between race-based  $eGFR \geq 60$  mL/min/1.73 m<sup>2</sup> and CV&P complications, our multivariable logistic regression model controlled for potential confounders. The results showed statistically significant 2.2 times higher odds of developing complications in a subgroup of Black patients who had race-dependent  $eGFR \geq 60$  mL/min/1.73 m<sup>2</sup> compared to an eGFR-matched subgroup of the non-Black cohort (Supplementary Table 1). Our study provides insights into the ongoing concerns of inequity and disparities associated with the historical use of race as a factor in the estimates of kidney functions. These findings critically evaluate the recent transition to race-free eGFR equations that prioritize individualized patient care and minimize disparities [24].

It is important to acknowledge that addressing racial disparities in healthcare extends beyond eGFR calculations [25, 26]. Factors such as socioeconomic status, access to health care, and cultural considerations, which tend to vary by race, also significantly impact patient out-

comes [27, 28]. Implementing a race-free approach to eGFR calculations is just one step towards ensuring more equitable healthcare [29, 30]. Further research is needed to delve deeper into the implications of removing race from eGFR equations in managing MIBC [31]. Prospective studies that evaluate long-term outcomes and survival rates in diverse patient populations can provide additional evidence to inform clinical guidelines and decision-making.

### Limitations

There are several limitations to consider in this study. It is important to note that an  $eGFR \geq 60$  mL/min/1.73 m<sup>2</sup> is not the sole determinant for clinical decision-making in the management of MIBC, and other cut-offs are also widely used [16, 32]. However, the stratification around an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup> is clinically important [33]. Additionally, this study is the first to evaluate the 30-day post cystectomy outcomes in a national cohort of MIBC patients stratified by an eGFR cut-off of 60 mL/min/1.73 m<sup>2</sup>. Similarly, our findings suggest a plausible association between CV&P complications and an RCM-based higher eGFR in MIBC patients. Finally, this study critically provides insights into the historical use of race-based equations in oncological practice.

### Conclusions

In conclusion, our study describes the potential implications of excluding race from the eGFR equation in managing MIBC. While race-based eGFR calculations may increase estimates of kidney function in MIBC patients, we observed higher 30-day post-cystectomy CV&P complications in a group of MIBC patients whose eGFR was  $\geq 60$  mL/min/1.73 m<sup>2</sup> due to the presence of the RCM. These findings underscore the need for further research to determine the implications of including race-based values in algorithms used in cancer care.

### Acknowledgements

Kathryn Hughes Barry had support from the National Cancer Institute (NCI K07 CA230182 and 3K07CA230182-05S1 to K.H.B.) and the Maryland Department of Health's Cigarette Restitution Fund Program - CH-649-CRF (salary support for K.H.B.) for this study.



**Disclosure of conflict of interest**

None.

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**Supplementary Table 1.** Univariate logistic regression model to estimate 30-day post-cystectomy cardiovascular and pulmonary complications between Black and Non-Black cohorts of MIBC patients

Cardiovascular & Pulmonary Complications	Odds ratio (95% conf. interval)	<i>p</i> -value
Non-Black (ref)		
Black	1.28 (0.93 - 1.77)	0.13