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Monocyte counts and prostate cancer outcomes in white and black men: Results from the SEARCH database

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Declaration: N/A

Compliance with ethical standards

Informed consent: The study protocol was approved by the institutional review boards of the Durham VA Health System and Cedars-Sinai Medical Center. Consent was obtained at time of entry to the study.

Research involving human participants and/or animals: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Abstract

Purpose: Circulating inflammatory markers may predict prostate cancer (PC) outcomes. For example, a recent study showed that higher peripheral blood monocyte counts were associated with aggressive PC in Asian men undergoing radical prostatectomy (RP). Herein, we investigated whether peripheral monocyte count can predict long-term PC outcomes after RP in black and white men.

Methods: We retrospectively reviewed data on 2,345 men undergoing RP from 2000 to 2017 at eight Veterans Affairs hospitals. Data on monocyte count within 6 and 12 months prior to surgery were collected. The study outcomes were biochemical recurrence (BCR), castration-resistant PC (CRPC), metastasis, all-cause mortality (ACM), and PC-specific morality (PCSM). Cox-proportional hazard models were used to assess the associations between pre-operative monocyte count and the above-mentioned outcomes accounting for confounders.

Results: Of 2,345 RP patients, 972 (41%) were black and 1,373 (59%) were white men. In multivariable analyses, we found no associations between monocyte count and BCR among all men (HR:1.36, 95%CI 0.90–2.07) or when analyses were stratified by race (HR:1.30, 95%CI 0.69–2.46, in black men; HR:1.33, 95%CI 0.76–02.33, in white men). Likewise, no overall or race-specific associations were found between monocyte count and CRPC, metastases, ACM, and PCSM, all p≥0.15. Results were similar for monocyte count measured at 12 months prior to RP.

Conclusion: In black and white PC patients undergoing RP, peripheral monocyte count was not associated with long-term PC outcomes. Contrary to what was found in Asian populations, monocyte count was not associated with PC outcomes in this study.

Keywords

Monocytes; prostate cancer; race

Introduction

Besides known risks factors for prostate cancer (PC) such as age and race, inflammation may also increase PC risk and progression (1). Accordingly, we and others found that anti-inflammatory medications such as aspirin and/or NSAIDs are associated with reduced PC risk (2, 3). Furthermore, a recent study found that aspirin use is also associated with reduced risk of PC mortality (4). If lower systemic inflammation is indeed a predictor of PC outcomes, one way of detecting inflammation to predict prognosis in PC patients is to measure blood markers of inflammation captured at the time of surgery. Recent retrospective studies in Asian men have identified a link between peripheral blood monocyte count and PC outcomes (5–7). In the first study, a high absolute monocyte count was linked to shorter overall and progression-free survival among 214 castration-resistant PC (CRPC) Japanese patients on first-line docetaxel chemotherapy (5). The second study showed that elevated serum monocyte levels were linked to aggressive PC and a greater likelihood of biochemical recurrence (BCR) in 248 Japanese patients who underwent radical prostatectomy (RP) (6). A third study among 290 Chinese men treated with androgen deprivation therapy (ADT), found higher monocyte count was associated with worse overall survival and PC-specific survival (7). If peripheral blood monocyte count were indeed identified as a biomarker for

PC outcomes, it would be a readily available tool since monocyte count data are routinely collected in clinical laboratories prior to surgery (7).

Previously, we investigated whether there was an association between pre-operative complete blood count (CBC) measures and long-term PC outcomes in white and black men who underwent RP (8). Except for a link between higher neutrophil count and all-cause mortality (ACM) in white men, no other associations were found between pre-operative CBC measures and PC long-term outcomes (8). In this study, we examined whether peripheral blood monocyte count was associated with PC outcomes within the Shared Equal Access Regional Cancer Hospital (SEARCH) database, a large cohort of patients who underwent RP (9). Based upon the prior data, albeit in men from Asia (5–7), we hypothesized that peripheral blood monocyte count at the time of RP is associated with worse short and long-term PC outcomes. Our primary outcome was biochemical recurrence (BCR), and our secondary outcomes were castration-resistant PC (CRPC), metastasis, ACM, and PC-specific mortality (PCSM). We also investigated how the association between peripheral blood monocyte count and long-term PC outcomes varied by race.

Materials and Methods

Study population and design

Data from PC patients undergoing RP between 2000 and 2017 at five Veteran Affairs Medical Centers (West Los Angeles and San Francisco, CA; Augusta, GA; Portland, OR and Durham NC) in SEARCH database where data on monocyte lab were complete were selected for analyses. Information on patients' age at the time of surgery, year of surgery, race, height, weight, pre-operative PSA levels, monocyte count and surgical specimen pathology (specimen weight, tumor grade, stage, seminal vesicle invasion, extracapsular extension, lymph node involvement, and surgical margin status) are contained in the database. Patients treated with androgen deprivation and/or radiation therapies prior to RP are not included in the database. Institutional review board approval was granted to the Durham IRB protocol which covers all participating institutions.

Of the 3,459, we excluded 866 men whose monocyte lab count were not collected within 1 year prior to RP. Of these, 817 were black (n=181) or white men (n=636). In addition, patients with race other than white or black (n=100) and those with missing covariates of interest (n=117) were excluded. To reduce the influence of extreme values, outlying values of monocyte count obtained using Tukey's method were excluded (n=31). Men excluded had similar clinical and demographic characteristics as the men included in the study, Supplementary Table 1. Our study population included 2,345 men (Figure 1).

Surgical outcomes

Primary outcome was BCR, defined as a single PSA > 0.2 ng/ml, two consecutive concentrations of 0.2 ng/ml, or secondary treatment for an elevated postoperative PSA. Secondary outcomes included CRPC, metastases, ACM, and PCSM. CRPC was defined as a PSA rise of ≥ 2 and ≥ 25% from the post-ADT nadir while being castrate, defined as testosterone < 50 ng/dL, bilateral orchiectomy, or continuous receipt of luteinizing hormone

releasing hormone agonist or antagonist. Development of metastases was determined radiographically as evidence of PC outside of the prostate, seminal vesicles, or pelvic lymph nodes. PCSM was defined based upon a review of the medical record showing metastatic progressive CRPC at time of death with no obvious indication of another cause of death. ACM included death from any cause.

Monocyte count

Pre-operative monocyte count within one year of surgery was ascertained from VA computerized medical records as monocyte count ($10^9/\mu L$).

Statistical analyses

Differences in demographic and clinicopathological factors between white and black men as well as among tertiles of monocyte count were appropriately examined using Wilcoxon rank-sum or Kruskal-Wallis tests for continuous variables, and chi-squared tests for categorical variables. Cox-proportional hazard (CPH) models were used to assess the association between pre-operative monocyte count and outcomes. Age-adjusted and multivariable CPH models were examined. Multivariable CPH models were adjusted for age at surgery (continuous), surgery year (continuous), race (black vs. white), VA center (8 centers), BMI (continuous, log-transformed), pre-operative PSA concentration (continuous; log-transformed), pathological grade group (1, 2–3, 4–5), extracapsular extension, seminal vesicle invasion, positive margins, and positive lymph node involvement. For our primary outcome, BCR, we examined monocyte count as a continuous and a categorical variable (categorized into tertiles). Monocyte count was examined as a continuous variable for secondary outcomes. The interaction between monocyte count and race was tested by including both main effects and a cross-product term in the model for all outcomes. As sensitivity analyses, we included only men with monocyte lab results within 6 months prior to RP and associations were re-examined.

With 1700 patients (equal number per group) adjusted for an anticipated event rate of 30%, we have 90% power at alpha significance level of 0.05 to detect a HR of 1.1.

Statistical analyses were performed using SAS 9.4 (SAS Cary, NC) and PASS 2020, v20.0.1. Statistical significance was two-sided $p<0.005$.

Results

Patient characteristics

Of the 2,345 RP patients with monocyte count within a year of surgery, 972 (41%) were black and 1,540 (59%) were white. Overall, white men higher monocyte count (0.6 vs. 0.5, $p<0.001$), were older (63 vs. 60, $p<0.001$) had lower pre-operative PSA (6.5 vs. 7.1, $p<0.001$), higher clinical stage ($p<0.001$), more extracapsular extension ($p=0.008$) and fewer positive surgical margins ($p=0.002$) than black men (Table 1a). Biopsy grade group was significantly different between the races ($p=0.002$), wherein white men appeared to have high grade (grade group, GG, 4–5) while lower grade tumors (GG 1, 2–3) were more common among black men. Similarly, white men had more tumors with higher pathologic

grade (GG 4–5) than black men (p<0.001). There was no statistically significant difference in BMI (p=0.470), seminal vesicle invasion (p=0.109) and lymph node involvement (p=0.416) between races. Among all men, median (IQR) follow-up time was 80 (46–132) months with white men having a longer follow-up time compared to black men (83 vs. 76 months, p=0.017). When demographic, clinical and pathologic characteristics were compared across tertiles of monocyte count, men in the lowest tertile of monocyte count had lower BMI and were less likely to have extracapsular extension (Table 1b). For all other factors, there was no difference across tertiles of monocyte count (all p≥0.070).

Primary outcome: biochemical recurrence

Overall, 786 men developed BCR during the follow-up period. Of these, 55% were white and 45% black. When examined as a continuous variable, on age-adjusted analysis, monocyte count was not associated with the risk of biochemical recurrence among the entire cohort (Hazard ratio (HR):1.08, 95% CI 0.72–1.63). In race specific analyses, no association was found between monocyte count and risk of BCR among black men (HR: 1.16 95% CI 0.62–2.17) or among white men (HR: 1.36 95% CI 0.78–2.35) (Table 2). In multivariable analysis, using continuous values of monocyte count, results were similar in that no association was found between monocyte count and BCR among the entire cohort (HR: 1.36 95%CI 0.90–2.07) or within each race stratum. Among all men and within each strata of race, when tertiles of monocyte count were examined, in both age-adjusted and multivariable models, no association was found between tertiles of monocyte count and biochemical recurrence (p≥0.226). There was no interaction between monocyte count and race (p≥0.760). On sensitivity analyses, when the analysis cohort was limited to 2,089 men with monocyte lab count within 6 months prior to RP, results remained the same in that no association was found between monocyte count and BCR. Likewise, there was no interaction between monocyte count and race (p≥0.880).

Secondary outcomes: CRPC, metastases, ACM, PCSM

Overall, 60 patients developed CRPC, 99 developed metastases, 389 died from any cause and 38 died from prostate cancer. In multivariable analyses, there was no statistically significant association between monocyte count and CRPC among all men (HR: 1.93, 95% CI 0.42–8.83), black men (0.26 (0.01–5.37) or white men (HR: 4.11, 95% CI 0.63–26.70) and no interaction was found between monocyte count and race (p=0.186) (Table 3). When association was examined among men with monocyte count within 6 months prior to RP, monocyte count was statistically significantly associated with CRPC (HR: 9.62, 95% CI 1.25–73.90) among white men but not among all (HR: 2.70, 95% CI 0.55–13.17) or black men (HR: 0.25, 95% CI 0.01–5.18). Again no interaction was found between monocyte count and race (p=0.115). Monocyte count was not associated with metastasis among all (HR: 1.89, 95% CI 0.58–6.16), black (HR: 1.10, 95% CI 0.15–8.20) or white (HR: 2.87, 95% CI 0.62–13.37) men. Similar results of no association was observed after sensitivity analyses including men with monocyte labs within 6 months prior to RP. On multivariable analyses, there was a statistically significant association between monocyte count and ACM among all (HR: 2.39, 95% CI 1.32–4.31) and white men (HR: 2.97, 95% CI 1.37–6.44) but not among black men (HR: 1.57, 95% CI 0.62–3.99) though there was no interaction between monocyte count and race (p=0.421). Results were Similar when men with

monocyte lab within 6 months of RP were included for analyses. Monocyte count was not associated with PCSM among all (HR: 4.36, 95% CI 0.62–30.70), black (HR: 0.51, 95% CI 0.01–36.06) or white (HR: 8.03, 95% CI 0.74–87.21) men. No interaction was found between monocyte count and race. After considering men with monocyte labs within 6 months prior to RP, there was an association between monocyte count and PCSM among white men (HR: 16.69, 95% CI 1.28–217.20).

Discussion

Inflammation is linked to the development and progression of PC (1), thus markers of systemic inflammation may predict disease course. To our knowledge, this is the first study to look at the relationship between peripheral monocyte count and PC outcomes in a racially diverse cohort including black men. We investigated whether peripheral monocyte count was associated with PC outcomes, specifically BCR, CRPC, metastases, ACM, and PCSM among 2,345 patients undergoing RP at eight VA hospitals. Overall, contrary to our hypothesis, no associations were found between peripheral monocyte count and PC outcomes in black and white men. Our results in the SEARCH database suggest that peripheral monocyte count may lack prognostic utility for PC patients who undergo RP.

Besides previous reports in Asian men which found positive associations between peripheral monocyte count and PC (5–7, 10), no other studies to date in white or black men have been reported. Wang et al. (7) found that among 1,107 Chinese men, monocyte count was higher in those who had a positive prostate biopsy compared to biopsy negative men. Similarly, Hayashi et al. (10), found that among all CBC parameters studied in 966 Japanese men undergoing biopsy, the monocyte fraction and monocyte-to-lymphocyte ratio were associated with high-grade PC, suggesting those patients would have worse PC prognosis. In a smaller cohort of 290 Chinese men treated with ADT as first-line therapy between 2010–2014 and followed-up for 37 months, a higher monocyte count was associated with increased risk of PCSM and ACM (7). In a separate study, among 248 Japanese men undergoing RP, higher peripheral blood monocyte count was a predictor of adverse pathology and BCR (6). Finally, a retrospective study among 214 castration-resistant PC patients treated with docetaxel in Japan, also found that elevated monocyte counts were associated with aggressive tumor features and poor overall survival (5). Of note, the monocyte counts range (Median 0.55, IQR=0.45–0.65) in our study were similar to those in the Chinese (7) (Median 0.45, IQR=0.36–0.56) and the Japanese (5) (Median 0.4, IQR=0.14–0.82) studies.

There are several reasons that could explain why the present results differ from those in Asian men. First, it is conceivable that racial differences in systemic inflammatory responses to PC tumors may exist. Although in this study, peripheral monocyte count prior to RP was similar in black and white men, we previously found significant racial differences in inflammatory cell make-up (8). For example, we found that among men undergoing RP, black men had more lymphocytes and fewer neutrophils (8) compared to white men, although as in the present study, no associations with PC outcomes were found. Second, in a previous study we found racial differences in intraprostatic inflammation among men undergoing prostate biopsies: Asian men had more, and black men had less acute

intraprostatic inflammation compared to white men (11). It is conceivable that circulating inflammatory markers may reflect local inflammation in the tumor. For example, previous work showed that peripheral blood monocyte count of Asian PC patients correlated with the number of tumor-infiltrating macrophages, which promote tumor growth and inhibit treatment response (6). However, while this had lent support to our hypothesis that peripheral monocyte count prior to RP would be associated with worse long-term PC outcomes in black and white men, our results did not support this hypothesis. Third, it is noteworthy that human monocytes can be subdivided into 3 classes, which have unique functional properties: classical, intermediate, and non-classical (12). This study did not distinguish between monocyte classes, so we cannot exclude the possibility that specific monocyte subtypes are associated with PC outcomes by race. Our finding that extracapsular extension (ECE) was less likely present among men in the lowest tertile for peripheral monocyte count is related to a previous finding that ECE was more likely observed in men with elevated peripheral monocyte count (6); however, ECE has low prognostic utility for men undergoing RP (13), which could explain why this finding did not have any bearing on PC outcomes.

We previously found that acute prostate inflammation was associated with lower PC risk at prostate biopsy (14). While classical monocytes are involved in both acute and chronic inflammation, there are data to suggest that nonclassical monocytes may play a more significant role in chronic inflammation (12); however, as mentioned above, this analysis does not differentiate between classical, intermediate and nonclassical monocyte types, given that we did not have that data. However, during inflammation associated with cancer, circulating monocytes leave the bloodstream and migrate into solid tissue tumors where they differentiate into macrophage or dendritic cell populations (12, 15). Thus, prostate tumors may induce local growth factors and pro-inflammatory cytokines to recruit monocytes and their maturation into tissue associated macrophages (TAMs) (12). TAMs can be divided into TAM1 and TAM2, depending on their pro- or anti-tumor activities (16, 17). Future studies are needed to elucidate how monocytes get recruited into prostate tumors and mature into either pro- or anti-tumor macrophages.

The many strengths of this study lie in the composition of the clinical research cohort, which was comprised of a large sample of RP patients, a high percentage of whom were black, and detailed, systematic follow-up of long-term outcomes post-RP. Our study was limited in its generalizability by the fact that lab data prior to 2000 was not readily available. Monocyte data were not available on all patients. This cohort of Veteran men, while ethnically diverse, presented mostly with pre-op and post-op GG 1–3 and clinical stage T1 PC, thus fewer men were included with more aggressive PC such as GG 4–5 (16%) and clinical stage T2/T3 (39%). Furthermore, the number of events for CRPC, metastasis, and PCSM was limited, particularly for stratified analysis by race, thus the null associations observed in this study should be confirmed in larger cohorts. Finally, while obtaining peripheral monocyte count provided a useful tool to understand how inflammation is related to PC outcomes, this study could have been improved by distinguishing between classical, intermediate, and non-classical monocyte types.

In conclusion, there were no associations between peripheral monocyte count and long-term PC outcomes among Veteran men undergoing RP, regardless of race. Our results do not suggest peripheral monocyte count to be an informative biomarker for PC long-term outcomes in black and white RP patients, but they do not exclude this possibility for Asian patients, a population in which associations between peripheral monocyte count and PC outcomes have been previously observed. Further studies of peripheral monocytes as a potential PC biomarker in Asian populations are warranted.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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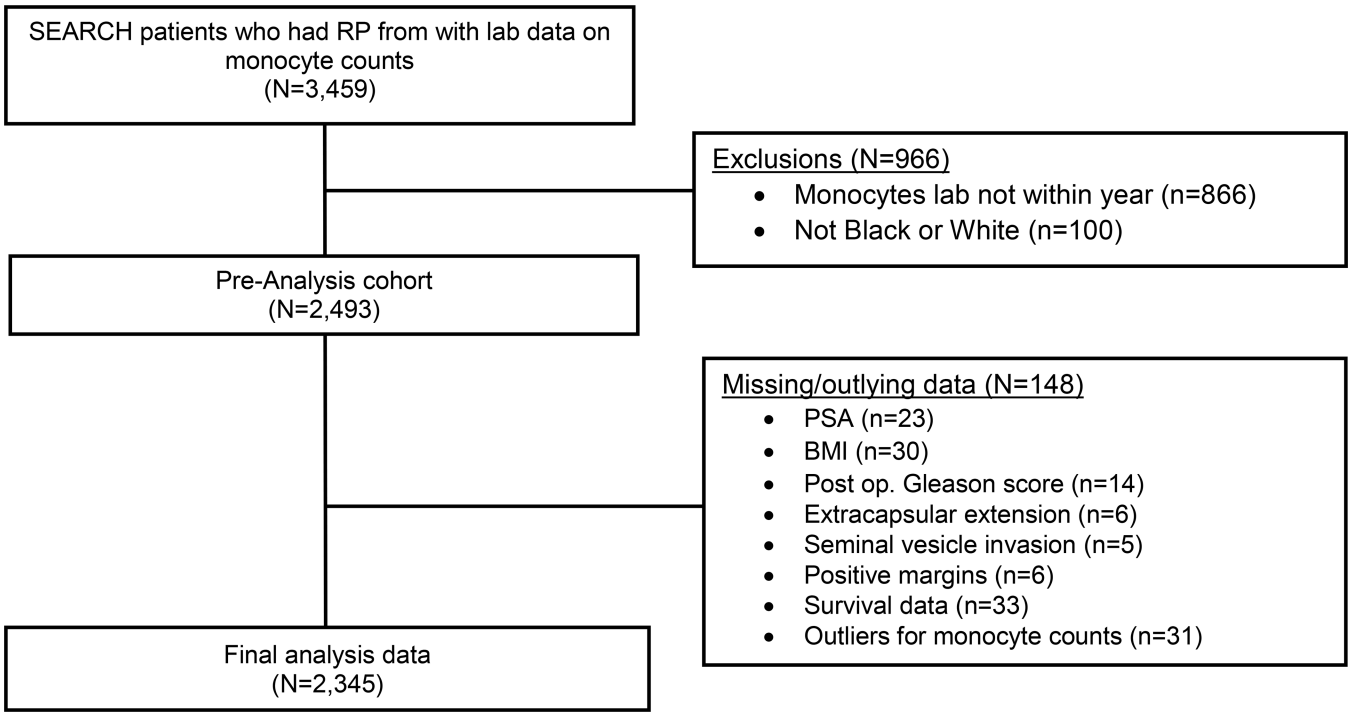

Figure 1:
Consort diagram showing patient selection

Table 1a:

Demographic, clinical and pathological characteristics of 2,345 RP study subjects by race

	Black men (N=972)	White men (N=1,373)	p value
[3]Age (years)	60 (56, 64)	63 (59, 67)	<0.001[1]
[3]BMI (kg/m^2)	28.1 (25.1, 31.7)	28.2 (25.5, 31.2)	0.470[1]
[3]PSA (ng/mL)	7.1 (5.1, 10.8)	6.5 (4.8, 9.5)	<0.001[1]
[3]Monocytes count (10^9/μL)	0.5 (0.4, 0.6)	0.6 (0.5, 0.7)	<0.001[1]
[3]Year of surgery	2010 (2005, 2013)	2010 (2004, 2013)	0.042[1]
[4]Pre-op grade group *			0.002[2]
1	360 (37%)	470 (34%)	
2–3	483 (50%)	642 (47%)	
4–5	128 (13%)	255 (19%)	
[4]Clinical Stage *			<0.001[2]
T1	687 (71%)	729 (53%)	
T2/T3	279 (29%)	611 (45%)	
[4]Post-op grade group			<0.001[2]
1	161 (17%)	280 (20%)	
2–3	695 (72%)	864 (63%)	
4–5	116 (12%)	229 (17%)	
[4]Extracapsular extension	208 (21%)	359 (26%)	0.008[2]
[4]Seminal vesicle invasion	138 (14%)	164 (12%)	0.109[2]
[4]Positive surgical margins	473 (49%)	578 (42%)	0.002[2]
[4]Lymph node involvement	32 (3%)	54 (4%)	0.416[2]
[3]Follow-up months after RP	76.7 (43.1, 127.7)	83.7 (47.6, 134.8)	0.017[1]

RP: radical prostatectomy, PSA: Prostate specific antigen, BMI: body mass index, Q1: 25th percentile; Q3: 75th percentile.

[1]Wilcoxon rank sum test

[2]Chi-square test

[3]Median (Q1, Q3)

[4]n (%).

*percentages may not add up to 100% because of missing values.

Table 1b:

Demographic, clinical and pathological characteristics of 2,345 RP study subjects by tertiles of monocyte count

	Tertile 1 (N=776)	Tertile 2 (N=894)	Tertile 3 (N=675)	p value
[3]Age (years)	62 (57, 66)	62 (58, 66)	62 (58, 66)	0.070[1]
[3]BMI (kg/m^2)	28.0 (25.4, 31.2)	28.2 (25.2, 30.9)	28.4 (25.5, 32.2)	0.038[1]
[3]PSA (ng/mL)	6.7 (4.9, 10.0)	6.6 (4.9, 10.2)	6.7 (4.9, 9.8)	0.908[1]
[3]Year of surgery	2010 (2005, 2013)	2010 (2004, 2013)	2010 (2005, 2013)	0.235[1]
[4]Pre-op grade group *				0.900[2]
1	283 (36%)	312 (35%)	235 (35%)	
2–3	372 (48%)	431 (48%)	322 (48%)	
4–5	120 (15%)	147 (16%)	116 (17%)	
[4]Clinical Stage *				0.146[2]
T1	497 (64%)	520 (59%)	399 (59%)	
T2/T3	266 (34%)	358(40%)	266 (39%)	
[4]Post-op grade group				0.697[2]
1	154 (20%)	169 (19%)	118 (17%)	
2–3	514 (66%)	586 (66%)	459 (68%)	
4–5	108 (14%)	139 (16%)	98 (15%)	
[4]Extracapsular extension	156 (20%)	224 (25%)	187 (28%)	0.003[2]
[4]Seminal vesicle invasion	98 (13%)	107 (12%)	97 (14%)	0.360[2]
[4]Positive surgical margins	348 (45%)	387 (43%)	316 (47%)	0.380[2]
[4]Lymph node involvement	21 (3%)	34 (4%)	31 (5%)	0.156[2]
[3]Follow-up months after RP	83.4 (47.3, 132.2)	82.7 (46.5, 138.8)	76.6 (43.1, 124.9)	0.141[1]

RP: radical prostatectomy, PSA: Prostate specific antigen, BMI: body mass index, Q1: 25th percentile; Q3: 75th percentile.

[1]Kruskal Wallis test

[2]Chi-Square test

[3]Median (Q1, Q3)

[4]n (%).

*percentages may not add up to 100% because of missing values.

Table 2:

Association between monocyte count (10^9/μL) and risk of biochemical recurrence (BCR) after RP among black and white men

BCR	All men (N=2,345)			Black men (N=972)			White men (N=1,373)			p^{int}
	events/n	HR (95% CI)	p-value	events/n	HR (95% CI)	p-value	events/n	HR (95% CI)	p-value	
Age adjusted model										
Tertile 1	264/776	ref	0.463	158/430	ref	0.962	106/346	ref	0.226	
Tertile 2	294/894	0.93 (0.79–1.10)		118/315	1.03 (0.82–1.31)		176/579	0.96 (0.75–1.22)		
Tertile 3	228/675	1.04 (0.87–1.24)		78/227	1.02 (0.78–1.34)		150/448	1.16 (0.90–1.48)		
Monocyte count	786/2345	1.08 (0.72–1.63)	0.686	354/972	1.16 (0.62–2.17)	0.636	432/1373	1.36 (0.78–2.35)	0.279	
*Multivariable model (with monocyte labs within 12 months prior to surgery)										
Tertile 1		ref	0.466		ref	0.920		ref	0.325	0.760
Tertile 2		0.96 (0.81–1.14)			1.05 (0.82–1.35)			0.90 (0.70–1.15)		
Tertile 3		1.07 (0.89–1.29)			1.03 (0.78–1.35)			1.06 (0.82–1.37)		
Monocyte count	786/2345	1.36 (0.90–2.07)	0.148	354/972	1.30 (0.69–2.46)	0.419	432/1373	1.33 (0.76–02.33)	0.321	0.897
*Multivariable model (with monocyte labs within 6 months prior to surgery)										
	All men (N=2,089)			Black men (N=902)			White men (N=1,187)			
Tertile 1	239/692	ref	0.533	145/399	ref	0.930	94/293	ref	0.419	0.880
Tertile 2	275/798	0.99 (0.83–1.18)		111/292	1.05 (0.81–1.35)		164/506	0.94 (0.73–1.22)		
Tertile 3	208/599	1.09 (0.90–1.32)		75/211	1.04 (0.78–1.38)		133/388	1.11 (0.84–1.45)		
Monocyte count	722/2089	1.44 (0.93–2.22)	0.104	331/902	1.37 (0.71–2.63)	0.346	391/1187	1.43 (0.79–2.58)	0.240	0.952

RP radical prostatectomy, BMI body mass index, PSA prostate specific antigen, HR hazard ratio, CI confidence intervals.

*Adjusted for: Age, Race, PSA (log transformed), BMI (log transformed), year of surgery, center, pathologic grade group, extracapsular extension, seminal vesicle invasion, surgical margins and Lymph node involvement.

Table 3:

Association between monocyte count (10^9/μL) and secondary outcomes** after RP among black and white men

	All men (N=2,345)			Black men (N=972)			White men (N=1,373)			p^{int}
	n	HR (95% CI)	p-value	n	HR (95% CI)	p-value		HR (95% CI)	p-value	
Age adjusted model										
CRPC	60	2.64 (0.64–10.92)	0.181	18	0.30 (0.02–5.59)	0.419	42	4.67 (0.86–25.45)	0.073	-
METS	99	2.29 (0.76–6.94)	0.143	37	0.96 (0.14–6.50)	0.967	62	3.71 (0.91–15.19)	0.068	-
ACM	389	2.11 (1.19–3.74)	0.011	159	1.69 (0.69–4.17)	0.253	230	2.95 (1.39–6.27)	0.005	-
PCSM	38	6.71 (1.18–38.34)	0.032	9	0.50 (0.01–29.28)	0.741	29	9.60 (1.28–71.95)	0.028	-
*Multivariable model(with monocyte labs within 12 months prior to surgery)										
CRPC	60	1.93 (0.42–8.83)	0.396	18	0.26 (0.01–5.37)	0.384	42	4.11 (0.63–26.70)	0.138	0.186
METS	99	1.89 (0.58–6.16)	0.290	37	1.10 (0.15–8.20)	0.924	62	2.87 (0.62–13.37)	0.180	0.462
ACM	389	2.39 (1.32–4.31)	0.004	159	1.57 (0.62–3.99)	0.344	230	2.97 (1.37–6.44)	0.006	0.421
PCSM	38	4.36 (0.62–30.70)	0.139	9	0.51 (0.01–36.06)	0.756	29	8.03 (0.74–87.21)	0.087	0.323
*Multivariable model (with monocyte labs within 6 months prior to surgery)										
	All men (N=2,089)			Black men (N=902)			White men (N=1,187)			
CRPC	55	2.70 (0.55–13.17)	0.221	18	0.25 (0.01–5.18)	0.368	37	9.62 (1.25–73.90)	0.029	0.115
METS	92	2.09 (0.62–7.10)	0.237	37	1.12 (0.15–8.39)	0.909	55	3.99 (0.74–21.44)	0.106	0.440
ACM	365	2.22 (1.20–4.12)	0.011	148	1.53 (0.58–4.08)	0.395	217	2.99 (1.33–6.76)	0.008	0.337
PCSM	36	5.74 (0.77–42.99)	0.089	9	0.50 (0.01–35.90)	0.753	27	16.69 (1.28–217.20)	0.032	0.254

** Secondary outcomes are: CRPC, METS, ACM and PCSM.

CRPC Castration resistant prostate cancer, METS Metastasis, ACM All-cause mortality, PCSM Prostate cancer specific mortality, RP radical prostatectomy, BMI body mass index, PSA prostate specific antigen, HR hazard ratio, CI confidence intervals

* Adjusted for: Age, Race, PSA (log transformed), BMI (log transformed, year of surgery, center, pathologic grade group, extracapsular extension, seminal vesicle invasion, surgical margins, and Lymph node involvement.