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## Neutrophil and Lymphocyte Counts as Clinical Markers for Stratifying Low-Risk Prostate Cancer

Young Suk Kwon<sup>1,2</sup>, Christopher Sejong Han<sup>3</sup>, Ji Woong Yu<sup>1,4</sup>, Sinae Kim<sup>1,2</sup>, Parth Modi<sup>3</sup>, Rachel Davis<sup>3</sup>, Ji Hae Park<sup>3</sup>, Paul Lee<sup>1</sup>, Yun-Sok Ha<sup>5</sup>, Wun-Jae Kim<sup>6</sup>, and Isaac Yi Kim<sup>1,3</sup>

<sup>1</sup>Section of Urologic Oncology, Rutgers Cancer Institute of New Jersey, Rutgers, The State University of New Jersey, New Brunswick, NJ

<sup>2</sup>Department of Biostatistics, Rutgers School of Public Health, Piscataway, NJ

<sup>3</sup>Division of Urology, Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ

<sup>4</sup>Sungkyunkwan University School of Medicine, Seoul, Korea

<sup>5</sup>Department of Urology, Kyungpook National University School of Medicine, Daegu, Korea

<sup>6</sup>Department of Urology, Chungbuk National University College of Medicine, Cheongju, Korea

### Abstract

Appropriate patient selection for active surveillance is challenging. Our study of 217 patients demonstrated that the preoperative absolute neutrophil and lymphocyte counts were better predictors of aggressive oncologic features than were the neutrophil-to-lymphocyte ratio in the assessment of low-risk prostate cancer patients. Our findings suggest that routine hematologic workup could be used to further stratify low-risk prostate cancer patients.

**Introduction**—The neutrophil-to-lymphocyte ratio (NLR) has emerged as a ubiquitous prognostic biomarker in cancer-related inflammation, specifically in patients with metastatic castration-resistant prostate cancer (PCa). We evaluated the clinical utility of the preoperative NLR, absolute neutrophil count (ANC), and absolute lymphocyte count (ALC) as a risk stratification tool for patients with low-risk PCa.

**Materials and Methods**—We identified 217 low-risk PCa patients with preoperative hematologic data who had met the criteria for active surveillance but had undergone robot-assisted radical prostatectomy at our institution from 2006 to 2015. Logistic regression models were constructed to determine whether the baseline NLR, ANC, and ALC were associated with upstaging, upgrading, and biochemical recurrence (BCR). Survival analyses were performed using the Kaplan-Meier method.

**Results**—On multivariate analysis, a higher prostate-specific antigen level (odds ratio [OR], 1.554; 95% confidence interval [CI], 1.148–2.104), a greater number of positive cores (OR, 2.098; 95% CI, 1.043–2.104), and a higher ALC (OR, 4.311; 95% CI, 1.258–14.770) were associated

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Address for correspondence: Isaac Yi Kim, MD, PhD, Section of Urologic Oncology, Rutgers Cancer Institute of New Jersey, Rutgers, The State University of New Jersey, 195 Little Albany St, New Brunswick, NJ 08903, kimiy@cinj.rutgers.edu.

### Disclosure

The authors have stated that they have no conflicts of interest.

with upstaging. More importantly, the 5-year biochemical recurrence-free survival was significantly lower in the high ANC group ( $ANC > 4.0 \times 10^9/L$ ) compared with that of the low ANC group ( $P = .011$ ). The NLR was not associated with upstaging, upgrading, or BCR in our study cohort ( $P = .368$ ,  $P = .573$ , and  $P = .504$ , respectively). The only significant association with upgrading was patient age (OR, 1.106; 95% CI, 1.043–1.173).

**Conclusion**—NLR was not useful in predicting adverse pathologic outcomes in our patients with low-risk PCa. However, relative neutrophilia and lymphocytosis might indicate an early manifestation of harboring a more aggressive PCa.

### Keywords

Active surveillance; Neutrophil-to-lymphocyte ratio; Pathological outcome; Prostate cancer; Radical prostatectomy

### Introduction

As a marker of cancer-related inflammation, the neutrophil-to-lymphocyte ratio (NLR) has become a clinically useful tool for predicting the response to therapy and prognosis in various types of malignancies.<sup>1</sup> Although the precise mechanism of inflammatory response in the tumor microenvironment remains to be elucidated, many studies have revealed that inflammation plays a key role in cancer development and its progression.<sup>2–4</sup> An elevated NLR indicates a high level of neutrophil-dependent inflammation with a concurrent reduction in the lymphocyte-mediated immune response, reflecting a carcinogenic milieu.<sup>5,6</sup> However, studies have also shown that tumor-infiltrating lymphocytes (TILs) are recruited to eradicate cancer cells in the early stages.<sup>7</sup> This would theoretically result in a lower NLR in the early stage of the disease. Adding further complexity, the temporal relationship between the increase in neutrophil and decrease in lymphocyte counts remains uncertain in the course of cancer progression.<sup>8</sup>

Despite our limited understanding of the mechanism, NLR has proved to be a valid prognostic biomarker in metastatic castration-resistant prostate cancer (mCRPC), with a higher NLR correlating with a worse prognosis.<sup>9</sup> In the context of localized prostate cancer (PCa), however, the role of the NLR and leukocyte subgroups has not been investigated. Because the understaging of patients considering active surveillance (AS) is a major concern, additional biomarkers are necessary to allow clinicians to better stratify patients who are considering AS.<sup>10</sup> Although the level of inflammation in low-risk PCa might not be as pronounced as that in mCRPC, we postulated that misclassified higher risk patients who meet the AS eligibility criteria could be detected using the aforementioned hematologic markers and that this information would supplement the current methods used in the risk stratification of patients with PCa.

The objective of our study was to evaluate the preoperative NLR, absolute neutrophil count (ANC), and absolute lymphocyte count (ALC) as independent predictors of adverse pathologic features, specifically upstaging, upgrading, and biochemical recurrence (BCR), among patients who would qualify for AS but who had undergone robot-assisted radical prostatectomy (RARP).

## Materials and Methods

### Patients

The present retrospective study was conducted using a prospectively maintained database of patients who had undergone RARP at the Rutgers Cancer Institute of New Jersey (RCINJ). Under an institutional review board-approved protocol, patients who met the AS criteria and had the complete blood count (CBC) with differential results available were selected for our analysis.

The RCINJ AS criteria are as follows: preoperative prostate-specific antigen (PSA) < 10 ng/mL, Gleason score  $\leq 6$  without grade 4 or 5, clinical stage  $\leq T2a$ ,  $\leq 3$  positive cores, and  $\leq 50\%$  cancer involvement in each positive core.<sup>11</sup> A single preoperative CBC with differential was performed as part of the routine preoperative assessment testing. The white blood cell (WBC) count, ANC, and ALC and their relative percentages were used in the present study. Our study patients first underwent prostate biopsy, followed by preoperative blood testing and then RARP. The pre-operative hematologic workup was performed approximately 2 weeks before RARP. In accordance with our institutional policy, a minimum 6 weeks of wait time was required for all patients undergoing RARP from the most recent prostate biopsy date. Only the CBC without differential was routinely performed at the follow-up visits.

The demographic data (eg, age, race, body mass index), PSA level, and pertinent biopsy findings and postoperative assessments, including pathologic Gleason score (PGS), pathologic stage, prostate weight, and BCR, were studied. Medical conditions (hematologic malignancy and diabetes mellitus) and medications (steroid, aspirin, and statin) that might have influenced the level of NLR were also assessed from the electronic medical record.<sup>12–15</sup>

In the present study, clinically significant upstaging was defined as any change in T stage from clinical T1–T2a to pathologic T3–T4. A PGS of 7 (both 3 + 4 and 4 + 3) and higher was considered as clinically significant upgrading. BCR was defined as an increasing PSA level on 2 consecutive measurements after RARP, with the last PSA value > 0.2 ng/mL.

The cutoff value of the NLR used for present analysis was 2.6, the median NLR in our study cohort. Previous studies have used a cutoff value of 2 to 3 because no single optimal value for baseline NLR has been established.<sup>16</sup>

### Statistical Analysis

All statistical analyses were performed using SPSS, version 21 (IBM Corp, Armonk, NY) and SAS, version 9.4 (SAS Institute, Cary, NC). *P* values < .05 were considered statistically significant. Comparisons between groups were performed using chi-square tests for categorical variables, and *t* tests and analysis of variance were used for continuous variables. Univariate and multivariate logistic regression analyses, adjusted for pertinent medical history and medications, were conducted to identify variables predictive of upgrading and upstaging. Survival analyses were performed using the Kaplan-Meier method with a log-rank test.

## Results

Of the 1137 patients analyzed, 217 patients met our institution's AS criteria but proceeded with RARP. With a median follow-up of 18.0 months, our study cohort was divided by the median NLR into high ( $\geq 2.6$ ) and low ( $< 2.6$ ) groups. Both groups had similar baseline demographic characteristics, except that the high NLR group had a greater proportion of white men (91.6% vs. 77.3%) and diabetes (10.3% vs. 2.7%) compared with the low NLR group ( $P = .012$  and  $P = .028$ , respectively; Table 1). With the exception of the preoperative hemoglobin levels ( $P = .275$ ), the preoperative NLR correlated with the various hematologic markers as expected, including the WBC counts, absolute and percentage of neutrophils, and absolute and percentage of lymphocytes ( $P < .0001$  for all). Although the likelihood of upstaging ( $P = .573$ ) and upgrading ( $P = .368$ ) were comparable in the high and low NLR groups, the distribution of the PGS was significantly different between the 2 groups, with patients with a GS  $\geq 8$  were exclusively found in the high NLR group ( $P = .019$ ).

In addition to the NLR, the ANC and ALC were assessed by dividing the study population at their median value of  $4.0 \times 10^9/L$  and  $1.52 \times 10^9/L$ , respectively (Table 2). On univariate analysis (Table 3), the common clinical parameters reported to be associated with upgrading and upstaging were selected and tested. The PSA level (95% confidence interval [CI], 1.044–1.739;  $P = .022$ ) and ALC (95% CI, 1.171–11.570;  $P = .026$ ) were significantly associated with upstaging. For upgrading, the only significant association was patient age (95% CI, 1.027–1.136;  $P = .003$ ). No medical conditions or medications were predictive of upgrading or upstaging.

A multivariate analysis model (Table 4) was constructed of the common demographic variables, pertinent medical conditions and medications, and variables with a  $P$  value  $< .05$  on univariate analysis. Multivariate analysis showed that a higher PSA (odds ratio [OR], 1.554; 95% CI, 1.148–2.104;  $P = .004$ ), a greater number of positive cores (OR, 2.098; 95% CI, 1.043–2.104;  $P = .038$ ), and a higher ALC (OR, 4.311; 95% CI, 1.258–14.770;  $P = .020$ ) were associated with upstaging. Patient age (OR, 1.106; 95% CI, 1.043–1.173;  $P = .001$ ), adjusted for other variables, was the only significant predictor of upgrading.

A total of 6 patients (2.8%) developed BCR in the course of their follow-up. The number of patients with BCR was not significantly different between the high NLR and low NLR groups ( $P = .504$ ; Figure 1A). We then examined ANC and ALC individually. When our study cohort was divided into high and low ANC groups, the biochemical recurrence-free survival (bRFS) of the high ANC group ( $\geq 4.0 \times 10^9/L$ ) was significantly lower than that of the low ANC group ( $< 4.0 \times 10^9/L$ ;  $P = .011$ ; Figure 1B). No significant difference was found in bRFS between the high ( $\geq 1.52 \times 10^9/L$ ) and low ( $< 1.52 \times 10^9/L$ ) ALC groups ( $P = .130$ ; Figure 1C).

## Discussion

In the present study, we investigated the potential role of NLR, ANC, and ALC as biomarkers to aid in identifying the few occult high-grade PCa cases in men who qualify for

AS. Our analysis showed evidence that relative neutrophilia and lymphocytosis, albeit at a subclinical level, predict for more aggressive PCa.

Although only 6 patients (2.8%) experienced BCR in our cohort during the study period, the 5-year bRFS rates were significantly different when the median ANC of  $4.0 \times 10^9/L$  was used. The high ANC group included all 6 patients with BCR, and the low ANC group had none ( $P = .011$ ). However, the patients in the low and high NLR groups were both found to have comparable BCR rates (3.6% vs. 1.9%;  $P = .504$ ). Similarly, no statistically significant difference was found in bRFS with different ALC levels ( $P = .130$ ; Figure 1). These findings suggest that a relatively high neutrophil level at an early stage of disease might be associated with more aggressive PCa. This hypothesis is consistent with findings from renal cell carcinoma for which neutrophilia is a validated independent risk factor for a poor prognosis.<sup>17</sup> Neutrophil-derived cytokines and proteins stored within granules have also been studied to predict tumor progression and severity in other types of cancers.<sup>18</sup> In the framework of prostate pathology, recent studies have linked elevated neutrophil counts in those with chronic prostatitis and other infectious diseases to an increased risk of developing PCa.<sup>19</sup>

In addition to the role of relative neutrophilia in tumor-related inflammation and the subsequently increased risk of BCR, our results revealed that relative lymphocytosis is associated with upstaging (OR, 4.872; 95% CI, 1.384–17.152;  $P = .014$ ). High ALCs are typically observed in viral infections<sup>20</sup>; however, no known relationships have been established with PCa. According to immunoediting during cancer development, Kim et al<sup>21</sup> described 3 distinct phases, the first of which involves complete elimination of tumor cells by T lymphocytes, explaining the relative lymphocytosis in the early-stage tumor. Moreover, in the study of prognostic significance of tumor-infiltrating lymphocytes (TILs) in localized PCa, Kärjä et al<sup>9</sup> analyzed the immunohistochemical characteristics of lymphocytes and concluded that strong expression of TILs was linked to perineural and capsular invasion ( $P = .017$  and  $P < .0001$ , respectively). Although the scope of our study precluded immunohistochemical analysis, we suspect that the increased levels of TILs in the high ALC group might have influenced the likelihood of upstaging. Notwithstanding these results, additional studies are necessary to further define the role of lymphocytosis in early-stage PCa, because the lymphocyte count was not associated with bRFS.

In contrast to the ANC and ALC, the NLR was not associated with upgrading, upstaging, or BCR ( $P = .368$ ;  $P = .573$ ; and  $P = .504$ , respectively). The univariate analysis constructed with NLR and other hematologic markers and other commonly associated clinical parameters also did not show a significant correlation of NLR with upgrading and upstaging. Although our small sample size might have contributed to this pattern, a possible explanation for this finding lies in the nature of our study cohort. Specifically, our patients had low-volume, low-grade cancer with a PSA upper limit of 10 ng/mL. The tumor burden of the patients in our study cohort might not have exceeded the threshold at which cancer-related inflammation becomes evident in the NLR. That most of our patients had an ANC and ALC within the reference ranges (92.6% and 98.6%, respectively) further suggests that only subclinical inflammatory responses, if any, were present in this cohort. The overall

upgrading and upstaging rates using our AS criteria were 26.7% and 8.3%, respectively. These rates are slightly lower than those from other previous studies using AS cohorts.<sup>22,23</sup>

The 6 patients with a high PGS (≥ 8) were found exclusively in the high NLR group ( $P = .019$ ), supporting the hypothesis that the NLR might be a potential inflammatory marker associated with more advanced cancer. Although multivariate and univariate analyses were not performed because of the small sample size, it should be noted that significant upgrading from a biopsy GS of 6 to a PGS of ≥ 8 is rare in men meeting the AS criteria.<sup>24</sup> Aggarwal et al<sup>4</sup> previously reported that a high NLR with high pro-inflammatory cytokines is more likely to occur in those with metastatic PCa. Although the NLR did not have a significant predictive value in our regression model, the association found between a high NLR and high-grade GS is consistent with the study by Ploussard et al<sup>25</sup> and provides ample support for further investigation of NLR.

The present study showed that a higher preoperative ANC and ALC, compared with the conventional NLR, were better predictors for worse clinicopathologic features, demonstrating their role in stratifying AS patients. We believe that the routine hematologic workup is immensely important in the era of AS, because sampling error during biopsy could place the patient in AS, missing the therapeutic window of intervention.<sup>25</sup> PSA remains the most widely used biomarker in predicting the aggressiveness of PCa. However, in an AS-eligible cohort, in which the variability of PSA is limited, leukocyte subgroups and NLR analysis might potentially offer additional parameters that can further stratify a seemingly homogenous group of patients. Although studies have also shown that the postoperative NLR is a prognostic marker for recurrence and measure of response to therapy in renal cell carcinoma,<sup>26,27</sup> our analyses for this project were limited to the preoperative setting to assess the cancer-related inflammation manifested in the pretreatment hematologic parameters.

Similar to NLR, the Glasgow prognostic score (GPS) used the combination of serum C-reactive protein with albumin as a prognostic and therapeutic indicator and has a decade of use and validation data across many types of cancer.<sup>28</sup> A study from a Scottish cancer registry, in particular, reported that the GPS is a prognostic indicator for the survival of patients with PCa.<sup>29</sup> It remains to be determined how the prognostic value of NLR, ANC, and ALC will compare with that of the GPS; however, it is certain that all these systemic inflammatory markers should continue to be studied in various cancer types.

The present study is the first, to our knowledge, that has attempted to elucidate the role of NLR, ANC, and ALC in low-risk PCa patients with histopathologic and clinical outcomes. In patients with low-grade PCa, we have concluded that a high ANC and ALC, respectively, correlate with biochemical recurrence and upstaging. We postulated that, unlike the positive associations found between the NLR and disease severity in other cancer settings, our patients might not have reached the critical point in disease progression such that the NLR would be significant. Nevertheless, our findings support the utility of ANC and ALC and that NLR should continue to be assessed to precisely define their roles in stratifying the risk of patients in AS.

The present study had several limitations. First, the retrospective study design we used is susceptible to hidden confounding variables. Second, our findings were from a single surgeon database at a tertiary surgical center and might not be generalizable to the general population of AS candidates. Third, although we adjusted for some potential confounders that might influence the level of neutrophils and lymphocytes in our multivariate regression model, it is unlikely that the reported values were solely attributed to PCa-related inflammation. Fourth, we did not adjust for the racial variation in NLR, despite the potential ethnic trends.<sup>30</sup> Fifth, the chance of a false-positive result (type I error) from multiple comparisons was not entirely negligible; thus, our results should be interpreted with caution. Sixth, the current usage of a single preoperative blood sample was less reliable and could be subject to fluctuation. Thus, our study findings could have been strengthened by different pre-operative sets of blood samples from each patient within a short period.

A multicenter prospective study would be ideal to further assess the utility of these hematologic markers. Also, as an extension to our research, these markers could be evaluated in the entire post-RARP cohort, stratified by relevant risk parameters, and a group of men actually undergoing AS. Finally, multiple postoperative CBCs with differential at different follow-up visits could potentially uncover important long-term patterns of oncologic control.

## Conclusion

Our present study has demonstrated that the baseline ANCs and ALCs are superior predictors of biochemical recurrence and upstaging, respectively, than the NLR in the assessment of low-risk PCa patients. When considering patients for AS, the presence of relative neutrophilia and lymphocytosis could be associated with increased risk. From our findings, we believe that routine hematologic workup could offer clinicians a ubiquitous cost-effective tool for further stratifying low-risk PCa patients considering AS.

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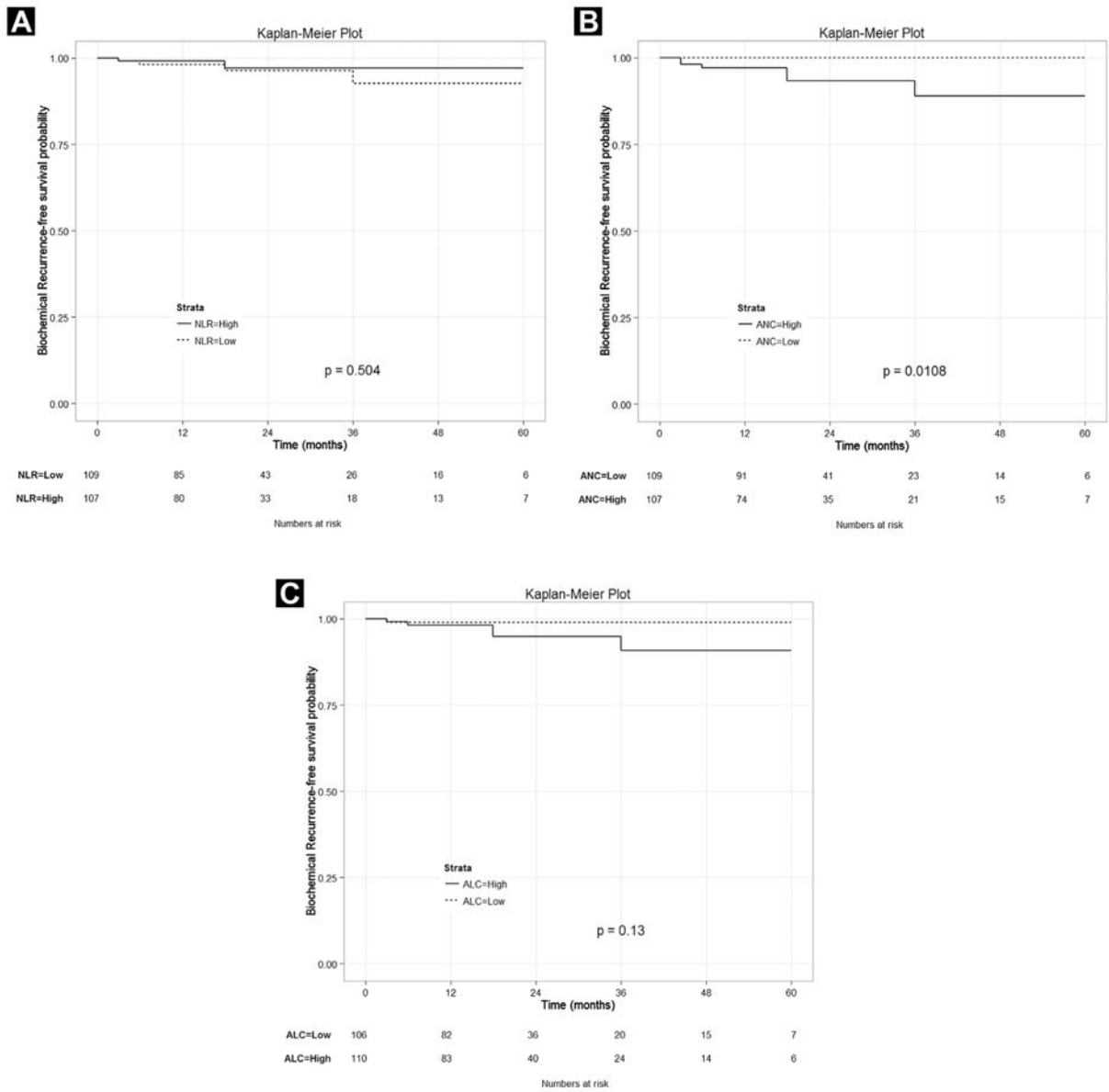
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### Clinical Practice Points

- The NLR has become a clinically useful marker for predicting the response to therapy and prognosis in different types of malignancies, including mCRPC.
- Because AS has become a widely accepted management option for localized PCa, appropriate patient selection is imperative to the management of safe and effective AS.
- Our study of 217 low-risk PCa patients who underwent RARP demonstrated that higher baseline ANCs and ALCs were associated with an increased risk of BCR and upstaging, respectively.
- Our study is noteworthy, because it attempted to elucidate the role of NLR, ANC, and ALC in low-risk PCa patients with the histopathologic and clinical outcomes.
- With further studies, a role might be shown for routine hematologic blood workup in assessing the level of cancer-related inflammation and stratifying low-risk PCa patients considering AS.



**Figure 1.** (A) Number of Patients With Biochemical Recurrence Was Not Significantly Different Between the High Neutrophil-to-Lymphocyte Ratio (NLR) and Low NLR Groups ( $P = .504$ ). (B) Biochemical Recurrence-Free Survival (bRFS) of High Absolute Neutrophil Count (ANC) Group ( $< 4.0 \times 10^9/L$ ) Was Significantly Lower Than That of Low ANC Group ( $< 4.0 \times 10^9/L$ ;  $P = .011$ ). (C) No Significant Difference Was Found in bRFS Between High ( $1.52 \times 10^9/L$ ) and Low ( $< 1.52 \times 10^9/L$ ) Absolute Lymphocyte Count (ALC) Groups ( $P = .130$ )

**Table 1**

## Baseline Characteristics of Patients Who Met AS Criteria and Underwent RARP

Characteristic	Total (n = 217)	NLR <2.6 (n = 110)	NLR ≥ 2.6 (n = 107)	P Value
Demographic characteristics				
Age (years)				.225
Median	59	58	60	
IQR	55–63	54–63	55–63	
Race (n)				.012
White	183 (84.3)	85 (77.3)	98 (91.6)	
African American	26 (12)	20 (18.2)	6 (5.6)	
Other	8 (3.7)	5 (4.5)	3 (2.8)	
BMI (kg/m <sup>2</sup> )				.062
Median	27.3	27.5	27.1	
IQR	25.2–30.1	26.1–30.5	25.0–29.4	
Preoperative PSA (ng/mL)				.935
Median	4.4	4.4	4.4	
IQR	3.6–5.9	3.7–5.7	3.6–6.2	
Positive core (n)				.815
1	110 (50.7)	54 (49.1)	56 (52.3)	
2	67 (30.9)	34 (30.9)	33 (30.8)	
3	40 (18.4)	22 (20.0)	18 (16.8)	
Maximum cancer in core (%)				.630
Mean	17.1	16.7	17.6	
Range	1–50	1–50	1–50	
Preoperative Gleason score				–
Median	6	6	6	
IQR	6–6	6–6	6–6	
Preoperative Hb (g/dL)				.275
Median	14.9	14.7	15.1	
IQR	14.2–15.6	14.2–15.3	14.1–15.7	
WBC count (×10 <sup>9</sup> /L)				<.0001
Median	6.4	5.7	7.0	
IQR	5.4–7.6	4.9–6.8	6.2–8.0	
Neutrophil (×10 <sup>9</sup> /L)				<.0001
Median	4.0	3.3	4.8	
IQR	3.2–5.0	2.6–3.9	4.1–5.7	
Lymphocyte (×10 <sup>9</sup> /L)				<.0001
Median	1.52	1.8	1.3	
IQR	1.25–1.88	1.5–2.2	1.1–1.5	

Characteristic	Total (n = 217)	NLR <2.6 (n = 110)	NLR ≥ 2.6 (n = 107)	P Value
Neutrophil (%)				<.0001
Median	63.0	57.7	69.3	
IQR	57.5–69.23	52.3–60.7	67.1–72.8	
Lymphocyte (%)				<.0001
Median	24.9	30.7	20.1	
IQR	20.2–30.8	27.6–34.8	17.2–22.3	
Clinical stage (n)				.174
T1	205 (94.5)	106 (96.4)	99 (92.5)	
T2a	12 (5.5)	4 (3.6)	8 (7.5)	
Medication and medical history (n)				
Aspirin				.664
No	149 (68.7)	74 (67.3)	75 (70.1)	
Yes	68 (31.3)	36 (32.7)	32 (29.9)	
Statin				1.00
No	138 (63.6)	70 (63.6)	68 (63.6)	
Yes	79 (36.4)	40 (36.4)	39 (36.4)	
Steroid				.618
No	214 (98.6)	109 (99.1)	105 (98.1)	
Yes	3 (1.4)	1 (0.9)	2 (1.9)	
Diabetes				.028
No	203 (93.5)	107 (97.3)	96 (89.7)	
Yes	14 (6.5)	3 (2.7)	11 (10.3)	
Hematologic malignancy				.984
No	215 (99.1)	109 (99.1)	106 (99.1)	
Yes	2 (0.9)	1 (0.9)	1 (0.9)	
Pathologic characteristics				
Pathologic stage				.573
T2	199 (91.7)	101 (91.8)	98 (91.6)	
T3a	18 (8.3)	9 (8.2)	9 (8.4)	
Pathologic Gleason score				.019
6	159 (73.3)	79 (71.8)	80 (74.8)	
7	52 (24.0)	31 (28.2)	21 (19.6)	
8	6 (2.8)	0 (0)	6 (5.6)	
Upstaging ( T3a)				.573
No	199 (91.7)	101 (91.8)	98 (91.6)	
Yes	18 (8.3)	9 (8.2)	9 (8.4)	
Upgrading (PGS ≥ 7)				.368
No	159 (73.3)	79 (71.8)	80 (74.8)	
Yes	58 (26.7)	31 (28.2)	27 (25.2)	

Characteristic	Total (n = 217)	NLR <2.6 (n = 110)	NLR ≥ 2.6 (n = 107)	P Value
Prostate weight (g)				.420
Median	49.0	49.0	48.0	
IQR	40.0–58.5	40.0–61.3	39.0–58.0	
Margin status				.549
Negative	189 (87.1)	96 (87.3)	93 (86.9)	
Positive	28 (12.9)	14 (12.7)	14 (13.1)	
Biochemical recurrence	6 (2.8)	4 (3.6)	2 (1.9)	.355

Data presented as n (%), unless otherwise noted.

Abbreviations: AS = active surveillance; BMI = body mass index; Hb = hemoglobin; IQR = interquartile range; NLR = neutrophil-to-lymphocyte ratio; PGS = pathologic Gleason score; PSA = preoperative prostate-specific antigen; RARP = robot-assisted radical prostatectomy; WBC = white blood cell.

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**Table 2**

Comparison of Upstaging and Upgrading Between High and Low ANC and ALC

Variable	Upstaging	Upgrading ( 3 + 4)	Upgrading ( 4 +9 3)
ANC			
<4.0	6 (5.6)	27 (25.0)	3 (2.8)
4.0	12 (11.0)	31 (28.4)	8 (7.3)
<i>P</i> value	.145	.567	.126
ALC			
<1.52	4 (3.8)	28 (26.4)	6 (5.7)
1.52	14 (12.6)	30 (27.0)	5 (4.5)
<i>P</i> value	.018	.919	.698

Data presented as n (%).

High and low groups divided by the median value.

Abbreviations: ALC = absolute lymphocyte count; ANC = absolute neutrophil count.

**Table 3**

Univariate Logistic Regression Analysis of Preoperative Parameters Predicting Upstaging and Upgrading

Parameter	Cutoff	Univariate <i>P</i> Value	
		Upstaging	Upgrading
Age (years)	–	.468	.003 <sup>a</sup>
Race	White vs. nonwhite	.581	.421
BMI (kg/m <sup>2</sup> )	–	.212	.795
Preoperative PSA (ng/mL)	–	.022 <sup>b</sup>	.102
Positive core	1 or 2 vs. 3	.097	.605
Hb (g/dL)	–	.887	.172
WBC ( $\times 10^9/L$ )	–	.075	.639
ANC <sup>c</sup> ( $\times 10^9/L$ )	<4.0 vs. 4.0	.132	.902
ALC <sup>c</sup> ( $\times 10^9/L$ )	<1.52 vs. 1.52	.026 <sup>d</sup>	.919
NLR <sup>c</sup>	<2.6 vs. 2.6	.951	.624
Aspirin	Yes vs. no	.734	.546
Statin	Yes vs. no	.777	.500
Diabetes	Yes vs. no	.872	.872

Abbreviations: ALC = absolute lymphocyte count; ANC = absolute neutrophil count; BMI = body mass index; CI = confidence interval; Hb = hemoglobin; OR = odds ratio; NLR = neutrophil-to-lymphocyte ratio; PSA = prostate-specific antigen; WBC = white blood cell.

<sup>a</sup>OR, 1.080; 95% CI 1.027–1.136.

<sup>b</sup>OR, 1.347; 95% CI, 1.044–1.739.

<sup>c</sup>Group divided at the median value.

<sup>d</sup>OR, 3.680; 95% CI, 1.171–11.570.



**Table 4**

Multivariate Logistic Regression Analysis of Preoperative Parameters Predicting Upstaging and Upgrading

Parameter	Cutoff	Multivariate <i>P</i> Value	
		Upstaging	Upgrading
Age (years) <sup>a</sup>	–	.168	.001 <sup>b</sup>
Race	White vs. nonwhite	.419	.609
BMI (kg/m <sup>2</sup> )	–	.120	.229
Preoperative PSA (ng/mL)	–	.004 <sup>c</sup>	.080
Positive core	1 or 2 vs. 3	.038 <sup>d</sup>	.176
ALC ( $\times 10^9/L$ ) <sup>a</sup>	<1.52 vs. 1.52	.020 <sup>e</sup>	.660
Aspirin	Yes vs. no	.342	.574
Statin	Yes vs. no	.584	.255
Diabetes	Yes vs. no	.762	.752

Abbreviations: ALC = absolute lymphocyte count; BMI = body mass index; CI = confidence interval; OR = odds ratio; PSA = prostate-specific antigen.

<sup>a</sup>Group divided at the median value.

<sup>b</sup>OR, 1.106; 95% CI, 1.043–1.173.

<sup>c</sup>OR, 1.554; 95% CI, 1.148–2.104.

<sup>d</sup>OR, 2.098; 95% CI, 1.043–2.104.

<sup>e</sup>OR 4.311; 95% CI, 1.258–14.770.