SYSTEMIC INFLAMMATORY RESPONSE AFTER TRANSRECTAL VS TRANSPERINEAL PROSTATE BIOPSY

[1]Gladwyn Ayudia Husain, [1]Kurnia Penta Seputra, [1]Taufiq Nur Budaya.

[1] Department of Urology, Faculty of Medicine/University of Brawijaya, Saiful Anwar Hospital, Malang.

ABSTRACT

Objective: *This study compares the inflammatory responses of TR and TP biopsies, using the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as biomarkers.****Material &Methods:*** *A retrospective cohort study was conducted at Dr. Saiful Anwar General Hospital, Malang, Indonesia, from January 2023 to August 2025, involving 46 patients who underwent TR or TP biopsies. Pre- and post-procedure blood samples were analyzed for NLR and PLR. Statistical analysis was performed using SPSS, employing paired t-tests and Mann-Whitney U tests.* ***Results:*** *NLR before the procedure was significantly higher in the TR group ($p = 0.034$). Post-procedure, there were no significant changes in NLR or PLR ($p > 0.05$). Infections and fever occurred more frequently in the TR group (12% and 24%, respectively), with no complications in the TP group. Prostate cancer detection rates were similar between both groups ($p = 0.760$).* ***Discussion:*** *Both biopsy methods induced systemic inflammation, as reflected by increased NLR and PLR post-procedure. However, TR biopsies were linked to a higher incidence of infections and febrile episodes. This aligns with prior studies indicating a greater complication rate with TR biopsies. NLR may serve as a potential biomarker for assessing tumor aggressiveness, especially in TR biopsy patients, where NLR changes were more pronounced among those diagnosed with prostate cancer.* ***Conclusion:*** *TP biopsies present lower infection risk and similar diagnostic accuracy compared to TR biopsies. NLR and PLR may be useful biomarkers for tracking inflammatory responses post-biopsy. Larger studies are needed to confirm these findings.*

Keywords: *Prostate cancer, prostate biopsy, transrectal biopsy, transperineal biopsy, NLR, PLR, inflammatory response, infection.*

ABSTRAK

Tujuan: *Studi ini membandingkan respons inflamasi dari biopsi TR dan TP, menggunakan rasio neutrofil-limfosit (NLR) dan rasio trombosit-limfosit (PLR) sebagai biomarker.* ***Bahan & Cara:*** *Sebuah studi kohortretrospektif dilakukan di Rumah Sakit Umum Dr. Saiful Anwar, Malang, Indonesia, dari Januari 2023 hingga Agustus 2025, yang melibatkan 46 pasien yang menjalani biopsi TR atau TP. Sampel darah sebelum dan sesudah prosedur dianalisis untuk NLR dan PLR. Analisis statistik dilakukan menggunakan SPSS, dengan menggunakan uji t-berpasangan dan uji Mann-Whitney U.* ***Hasil:*** *NLR sebelum prosedur secara signifikan lebih tinggi pada kelompok TR ($p = 0,034$). Setelah prosedur, tidak ada perubahan signifikan pada NLR atau PLR ($p > 0,05$). Infeksi dan demam terjadi lebih sering pada kelompok TR (masing-masing 12% dan 24%), tanpa komplikasi pada kelompok TP. Tingkat deteksi kanker prostat serupa antara kedua kelompok ($p = 0,760$).* ***Diskusi:*** *Kedua metode biopsi tersebut menginduksi peradangan sistemik, yang tercermin dari peningkatan NLR dan PLR setelah prosedur. Namun, biopsi transrektal (TR) dikaitkan dengan insiden infeksi dan episode demam yang lebih tinggi. Hal ini sejalan dengan penelitian sebelumnya yang menunjukkan tingkat komplikasi yang lebihtinggi pada biopsi TR. NLR dapat berfungsi sebagai biomarker potensial untuk menilai agresivitas tumor, terutama pada pasien biopsi TR, di mana perubahan NLR lebih menonjol di antara mereka yang didiagnosis menderita kanker prostat.* ***Simpulan:****Biopsi transperineal (TP) menunjukkan risiko infeksi yang lebih rendah dan akurasi diagnostik yang serupa dibandingkan dengan biopsi TR. NLR dan PLR mungkin merupakan biomarker yang berguna untuk melacak respons inflamasi pasca-biopsi. Studi yang lebih besar diperlukan untuk mengkonfirmasi temuan ini.*

Kata kunci: *Kanker prostat, biopsi prostat, biopsi transrektal, biopsi transperineal, NLR, PLR, respons inflamasi, infeksi.*

Correspondence: Gladwyn Ayudia Husain; c/o: Department of Urology, Faculty of Medicine, Universitas Brawijaya, Saiful Anwar General Hospital. Jl. Jaksa Agung Suprapto No.2, Klojen, Kec. Klojen, Malang, Jawa Timur 65112, Indonesia. Fax: +62341333030. Email: gladwynhusain@gmail.com.

INTRODUCTION

Prostate cancer (PC) ranks sixth as the leading cause of cancer death in men worldwide and is the most commonly diagnosed malignancy in men.[1] In 2020, there were 1.466.680 new cases of this disease diagnosed worldwide, resulting in 396.792 deaths annually.[2] Based on 2022 data, prostate cancer in Indonesia ranks fifth after lung, colorectal, liver, and nasopharyngeal cancer with 13.130 new cases. The mortality rate reaches 2% or ranks 12th among other cancers.[3]

Prostate cancer diagnosis is primarily established through histopathological evaluation of tissue specimens obtained via surgical procedures such as transurethral resection of the prostate (TURP) and prostatectomy, as well as through prostate biopsy.[4] Among diagnostic modalities, prostate biopsy remains the definitive standard for confirming the presence of malignancy in cases of clinical suspicion.[3] In recent years, transperineal (TP) prostate biopsy has gained increasing clinical adoption owing to its lower incidence of infectious complications and enhanced diagnostic accuracy, particularly for tumors located in the anterior prostate lobe, when compared to the transrectal (TR) approach.[5] Numerous studies have aimed to compare the detection efficacy and complication profiles of TR and TP biopsy techniques. Evidence indicates that TP biopsy significantly decreases infection-related adverse events relative to TR biopsy.[6-7] and it demonstrates superior detection rates for anterior zone tumors.[8-9] Despite these differences, most research reports no statistically significant disparity between TR and TP approaches regarding overall cancer detection rates and cancer core yield. Nevertheless, the diagnostic performance of both methods may be influenced by patient-specific factors such as age, prostate-specific antigen (PSA) levels, and prostate volume, which can lead to variations in detection rates across different patient populations.[10-11]

Transperineal biopsy (TP) has a lower risk of infection complications, particularly sepsis and urinary tract infections, compared to transrectal biopsy (TR), with similar diagnostic accuracy. However, TP biopsy may be associated with a slightly higher risk of urinary retention and periprocedural discomfort, although these differences are generally minor and self-limiting.[12]

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inflammatory biomarkers that are widely used as prognostic indicators for various diseases.[13,14] NLR and PRL are considered cost-effective and easily measurable indicators of inflammation. Neutrophilia and lymphopenia are considered the main mediators of systemic inflammation.[15] Biologically, the inflammatory process plays a crucial role in the development of prostate cancer through mechanisms such as oxidative stress, increased angiogenesis stimulation, and changes in the tumor microenvironment.[16] Several studies have examined the possibility of prostate cancer or its severity, but the results of various studies still show differences.[17-18]

Research by Gokce et al. in 2016 revealed that a high NLR prior to biopsy was associated with prostate cancer risk, while another study conducted by Tang et al. in 2023 found no significant association.[17-18] Therefore, the diagnostic value of NLR and PLR in patients undergoing prostate biopsy remains debatable.

Currently, studies evaluating NLR and PLR values in patients undergoing prostate biopsy, both TR and TP, are still limited. Therefore, it is important to conduct research related to the evaluation of NLR and PLR in prostate biopsy before and after transrectal (TR) and transperineal (TP) transrectal ultrasound-guided procedures, as this can be a consideration in choosing the biopsy method to be used and post-procedure complications, as well as a consideration for suspected prostate malignancy.

OBJECTIVE

This study compares the inflammatory responses of TR and TP biopsies, using the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as biomarkers.

MATERIAL &METHOD

This retrospective cohort study was conducted at Dr. Saiful Anwal Regional General Hospital in Malang, Indonesia, from January 2023 to August 2025. This study was approved by the Dr. Saiful Anwar Malang Clinical Research Ethics Committee with number 400/332/K.3/102.7/2025 and written consent was obtained from all participants.

Data related to respondent characteristics and the study were collected using secondary medical records. Data were obtained from patients who underwent prostate biopsy. Inclusion criteria included patients who underwent TR or TP prostate biopsy and had routine blood tests before and after the procedure. As this was a pilot study, no exclusion criteria were used. Patients with comorbidities such as diabetes mellitus, hypertension, and vertebral fractures were included in the study because this study assessed changes in systemic inflammatory markers. NLR values were measured using the formula: Number of Neutrophils divided by Number of Lymphocytes, while PLR was measured using the formula: Number of Platelets divided by Lymphocytes at the Clinical Pathology Laboratory of Dr. Saiful Anwar Regional General Hospital in Malang, with samples collected in EDTA tubes 1 day before and 1 day after the biopsy procedure.

Statistical analysis was performed using SPSS 24.0 for Windows software, with NLR and PLR values presented as mean ± standard deviation. Demographic data were reported as frequency and percentage. Differences in NLR and PLR values between groups were analyzed using the unpaired t-test if the data were normally distributed and the Mann-Whitney U test for data that were not normally distributed, while differences in demographic data were tested using the chi-square test. Statistical significance was set at a p-value <0.05.

RESULTS

This study involved 46 patients who underwent prostate biopsy, including 21 samples using the transperineal approach and 25 using the t ransrectal approach. The demographic characteristics of the samples are shown in Table 1. All patients underwent urine culture before and after biopsy. No bacterial growth was found in any of the urine samples, but in patients who underwent transrectal biopsy, 3 patients (12%) had Escherichia coli bacterial growth, and 6 (24%) experienced fever after the biopsy procedure. In the transperineal biopsy group, no bacterial growth was found in urine cultures, and no fever was observed after the procedure.

Table 1. Respondent Characteristics.

Characteristics	Category	Transperineal Biopsy (n= 21)	Biopsy Transrectal (n=25)	P value
Age	Mean ± Standard Deviation	64.5 ± 8.1	67.8 ± 9.3	0.253
Prostate Volume	Mean ± Standard Deviation	63.24 ± 23.30	55.55 ± 28.65	0.774
PSA Level at Biopsy	Mean ± Standard Deviation	64.5 ± 8.1	67.8 ± 9.3	0.614
BMI	Underweight/Normal Weight	12 (57.1)	10 (40.0)	0.375
	Overweight/obesity	9 (42.9)	15 (60.0)	
PA results	Prostate Cancer	13 (61.9)	17 (68.0)	0.760
	BPH	8 (38.1)	8 (32.0)	
Gleason Score	7	3 (23.1)	3 (17.6)	
Classification (In Prostate Cancer Biopsy)	8-10	10 (76.9)	14 (82.4)	1
Core biopsy rate (In biopsies with prostate cancer)	Mean ± Standard Deviation	6.30 ± 4.11	6 ± 3.2	0.133
Pain score after the procedure (VAS)	Median ± Interquartile range	1	1±1	0.258

*Independent T-test

Table 2. PLR and NLR values before, after, and increase after treatment.

Characteristics	Category	Transperineal Biopsy (n= 21)	Biopsy Transrectal (n=25)	P value*
NLR Before Intervention	Mean ± Standard Deviation	1.98 ± 0.38	2.67 ± 0.62	0.034
NLR After Intervention	Mean ± Standard Deviation	2.44± 0.49	3.28± 0.72	0.793
NLR Change	Mean ± Standard Deviation	0.45± 0.12	0.60 ± 0.16	0.067
PLR Before Intervention	Mean ± Standard Deviation	129.39 ± 19.4	145.59 ± 26.4	0.158
PLR After Intervention	Mean ± Standard Deviation	158.58 ± 25.4	178.99 ± 33.85	0.184
Change in PLR	Mean ± Standard Deviation	29.19 ± 8	33.40 ± 10.05	0.167

*Independent T-test

Table 3. PLR and NLR values before, after, and during improvement in transperineal biopsy based on PA diagnosis

Characteristics	Category	Prostate Carcinoma (n= 13)	Non-Carcinoma (n=8)	P value*
NLR Before Intervention	Mean ± Standard Deviation	2.03 ± 0.25	1.89 ± 0.55	0.097
NLR After Intervention	Mean ± Standard Deviation	2.50± 0.33	2.33 ± 0.68	0.092
Change in NLR	Mean ± Standard Deviation	0.47± 0.09	0.43 ± 0.16	0.125
PLR Before Intervention	Mean ± Standard Deviation	132.33 ± 17.9	124.61 ± 22.09	0.642
PLR After Intervention	Mean ± Standard Deviation	162.10± 22.6	152.85 ± 30.10	0.366
Change in PLR	Mean ± Standard Deviation	29.77 ± 6.83	28.24 ± 15.77	0.181

*Independent T-test

Table 4. PLR and NLR values before, after, and increase in transrectal biopsy based on PA diagnosis

Characteristics	Category	Prostate carcinoma (n= 17)	Non-Carcinoma (n=8)	P value*
NLR Before Intervention	Mean ± Standard Deviation	2.78 ± 0.72	2.68 ± 0.61	0.725
NLR After Intervention	Mean ± Standard Deviation	3.43 ± 0.74	3.24± 0.74	0.649
Change in NLR	Mean ± Standard Deviation	0.64 ± 0.06	0.55 ± 0.18	<0.001
PLR Before Intervention	Mean ± Standard Deviation	161.21 ± 25.08	156.37 ± 33.04	0.251
PLR After Intervention	Mean ± Standard Deviation	200.43 ± 33.59	189.27 ± 40.28	0.520
Change in PLR	Mean ± Standard Deviation	39.21 ± 12.07	32.90 ± 10.69	0.268

*Independent T-test

DISCUSSION

This study presents a new review of the relationship between the type of prostate biopsy and changes in inflammatory markers in routine blood tests. Ultrasound-guided biopsy with a transperineal approach is recommended because it has a lower risk of infection.[7] In this study, we found E. coli infection in the urine after biopsy and approximately 24% experienced fever. This is in line with other studies that the risk of infection in transrectal biopsy is higher than in transperineal biopsy.[19-20] Urinary tract infection is the most common complication after prostate biopsy, with an incidence rate ranging from 0.1% to 7%. On the other hand, the risk of sepsis ranges from 0.3% to 3.1%.[21] A study of bacterial cultures from patients with prostatitis after biopsy showed that 80% of cases were caused by E. coli strains.[22]

One strategy for preventing infection in prostate biopsies is the administration of prophylactic antibiotics. The Japanese Urology

Association recommends oral Levofloxacin or aminoglycosides, while the American Urology Association recommends first/second generation cephalosporins ± aminoglycosides or third generation cephalosporins.[23-24] The European Urology Association recommends fluoroquinolones if there are no contraindications.[25] A randomized controlled trial found that additional prophylaxis with a single dose of gentamicin is a practical approach and recommends culture-based prophylaxis if there are contraindications to the use of gentamicin.[26] In this study, all samples received prophylactic therapy with a single 160 mg dose of gentamicin in the transrectal biopsy group and 1000 mg of ciprofloxacin or a single 160 mg dose of gentamicin in the transperineal group.

This study found an increase in NLR and PLR before and after biopsy with both TP and TR methods, but the two were not significantly different. This indicates systemic inflammation but does not significantly cause sepsis. In this study, there was also 1 patient with sepsis in the TR procedure who experienced a threefold increase in NLR after biopsy compared to before biopsy. This is consistent with the study by Bennet et al. in 2015, where the incidence of sepsis was 0.8% in TR biopsies compared to 0.1% in TP biopsies.[27]

Additionally, this study found higher increases in NLR and PLR values in the TR group compared to the TP group, although the differences were not significant. This increase was due to the fact that transrectal biopsy (TR) involves needle penetration through the rectal mucosa into the prostate gland, allowing intestinal bacteria or rectal flora (including Escherichia coli) to migrate to the prostate tissue, urinary tract, or bloodstream and trigger a systemic inflammatory reaction.[27]

In the subgroup analysis, a significant difference was found in the change in NLR values before and after TR biopsy in patients with prostate carcinoma compared to non-carcinoma ($P < 0.001$). A study conducted by Gokce et al. in 2015 revealed that NLR was higher in individuals with prostate cancer compared to patients with benign prostatic hyperplasia (BPH), and increased NLR was associated with higher Gleason scores, indicating increased tumor malignancy.

Tumors with higher malignancy tend to produce more inflammatory mediators that increase the number of neutrophils. More aggressive tumors can also cause more damage to tissues, thereby increasing inflammation. In addition, prostate biopsies, especially transrectal biopsies (TRUS), can cause local damage and inflammation to prostate tissue. In individuals with prostate cancer, this inflammation becomes more intense due to the presence of the tumor. Thus, the number of neutrophils will increase in response to tissue damage, while lymphocytes do not play a significant role, resulting in a higher NLR increase after biopsy in patients with prostate cancer compared to patients without prostate cancer.[28]

The neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) are inflammatory biomarkers that are widely used as prognostic indicators for various diseases.[13-14] NLR and PRL are considered cost-effective and easily measurable indicators of inflammation. Neutrophilia and lymphopenia are considered the main mediators of systemic inflammation.[15] Currently, there are no studies related to NLR and PLR in patients after transrectal or transperineal biopsy for prostate cancer. This study shows that there is no difference in inflammatory response between the two biopsy techniques, and there is also no significant difference in pain after the procedure. Eren's study showed that increased NLR can be a predictive risk factor for prostate cancer, but in this study, we found that NLR and PLR were not associated with prostate cancer ($p=0.573$ and $p=0.542$).

This is also in line with the 2023 Randomized Controlled Trials Mian et al. study, which reported no significant differences in post-biopsy infection complications between the TP and TR groups.[29]

The limitations of this study include a limited sample size, which may introduce potential bias. Additionally, fractures and other comorbidities may influence NLR and PLR values in the sample.

CONCLUSION

In this study, there was no difference in changes in NLR and PLR after prostate biopsy using the transrectal and transperineal approaches; however, complications such as infection and fever were more common in transrectal biopsy, with significant changes in NLR and PLR in the group with sepsis after TR biopsy.

In TR biopsy, there was a significant increase in NLR in prostate carcinoma compared to the non-carcinoma group.

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