Original Article | Iran J Pathol.2018; 13(3):333-339

Iranian Journal of Pathology | ISSN: 2345-3656

Prognostic Value of Neutrophil to Lymphocyte Ratio on Pathologic Findings of Transrectal Ultrasonography Guided Biopsy of Prostate

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KEYWORDS

Neutrophil/Lymphocyte Ratio,
Prostate,
Pathology,
Biopsy

Article Info

Received 09 March 2017;
Accepted 18 Aug 2018;
Published Online 12 Sep 2018;

ABSTRACT

Background and Objective: Prostate cancer is considered as one of the most common malignancies in males. Despite the decreasing trend during the past decade, the incidence continues to rise in adolescents worldwide. Recently, new emerging technologies beside TRUS-guided prostate biopsy were introduced and showed high potential in the diagnosis of prostate cancer. The current study aimed at investigating the role of blood cell count and its prognostic value on pathologic findings.

Methods: The current prospective analysis was conducted on patients with abnormality from January 2013 to January 2016. A total of 168 CBC tests including absolute Neutrophil and lymphocyte counts were performed on males at the Department of Urology, Razi University Hospital (Guilan, Iran). Of these, all males had both CBCs and free:total (F/T) prostate-specific antigen (PSA) ratio.

Results: Average age of patients was 63.5±7. It was observed that Neutrophil count and Neutrophil percentage was not significantly different among the groups with different pathologies. In comparison to biopsy findings none of the cell count had suitable specificity and sensitivity. In the multivariate analysis to predict malignancy, only age (B=0.1, S.E=0.04, EXP [B]) =1.1 and sig=0.00) and PSA level (B=0.1, S.E=0.04, EXP [B]) =1.1 and sig=0.00) were significant.

Conclusions: In comparison to biopsy findings, none of the cell counts (absolute or percent) had suitable specificity and sensitivity, and the cell count and percentage before biopsy were not different among the groups with different pathologies. Powerful and long-term studies are required to evaluate prognostic values of cell count on adenocarcinoma.

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Introduction

Prostate cancer is considered as one of the most common malignancies in males (1). About 14% of males are diagnosed with prostate cancer sometime through their lifespan (2). Despite the decreasing trend of the prostate cancer during the last 10 years, there is an increase in incidence of the prostate cancer among adolescents (3).

Up to now the gold standard to detect prostate adenocarcinoma in patients suspected to prostate cancer is systematic standard transrectal ultrasound (TRUS)-guided biopsy of the prostate (4).

The current study aimed at finding any relationships between the neutrophil count and neutrophil/lymphocyte ratio to the pathologic reports of the TRUS-guided biopsy of the prostate. The study also sought to find their prognostic values.

Material and method

Patients

The current prospective analysis was conducted on patients from January 2013 to January 2016.

After receiving permission from the Research Ethics Board (REB) of our hospital, a total of 168 complete

blood count (CBC) tests including absolute neutrophil and lymphocyte counts were performed on males at the Department of Urology, Razi University Hospital (Guilan, Iran). Of these, all males had both CBCs and free: total (F/T) prostate-specific antigen (PSA) ratio. The study also investigated subjects undergoing TRUS-guided biopsy of the prostate with abnormal digital rectal exam or PSA levels in suspicious range. The current study protocol was approved by the Institutional Review Board of Guilan University of Medical sciences, Rasht, Iran.

The exclusion criteria were: known malignancy other than prostate, history of local or systemic infection, any medication related to inflammatory condition of patient such as corticosteroids and hematologic dyspraxia.

Clinical and laboratory assessments

Blood samples were collected one day before biopsy and after antibiotic prophylaxis. Total WBC, neutrophil, and lymphocyte counts were reported by Sysmex XE-2100 Hematology Analyzer (Sysmex Corp., Kobe, Japan). Neutrophil-to-lymphocyte ratio (NLR), absolute neutrophil count was defined by dividing absolute lymphocyte counts. CRP levels were measured by means of automated latex-enhanced turbid metric immunoassay (Dimension; Dade Behring, Newark, NJ, USA; TBA-200FR; Toshiba, Tokyo, Japan) in the first hour after sampling.

Two experienced pathologists with more than five years of experience to diagnose prostate pathology reviewed the specimens to verify the diagnosis. The Gleason score (GS) grading system, 2010 update, was used to grade prostate (5).

Treatment

A urology PGY-4 resident with satisfactory experience in TRUS-biopsy performed all the prostate biopsies in the study. All patients were prepared with spinal anesthetics using a BK ultrasound scanner, end fire transducer, a needle guide, and an 18-G 25-cm biopsy needle; after undergoing ciprofloxacin prophylaxis for three days, the treatment regimens provided to patients remained consistent over the study era.

If pathology was anything other than benign prostatic hyperplasia (BPH) and patient underwent a radical prostatectomy, then the final pathology (and its GS) was considered in the data (13 patients).

Statistical analysis

Patients` demographics were compared between patients with positive and negative prostate adenocarcinoma. Patient with NLR and neutrophil count were also assessed for differences in different pathologic groups. Statistical tests used for the aforementioned univariate analyses included independent samples t test or the Mann Whitney U test for continuous variables and $\chi 2$ or the Fisher exact test for categorical variables, where applicable.

The exploratory variables analyzed in univariate and multivariable survival analyses were assessed as follows: age (continuous), CBC count, NLR ratio, PSA (0.4 to 88 ng/mL), and CRP level.

The cut off points of NLR were determined according to the sensitivity and specificity levels derived from the area under receiver operator characteristics (AUROC) curve plotted using the presence or absence of prostatic carcinoma.

Statistical tests were two sided with α significance level of 0.05. All analyses were performed with SPSS version 20.

Results

Basic characteristics

From October 2013 to march 2016, 168 biopsies were undertaken on 168 patients. The mean age of patients was 63. 5±7 years; their first PSA level was 11.6±10.1 ng/mL in average and after mean four weeks of taking anti-inflammatory by all patients, and antibiotic therapy in 89 patients (53%) PSA reached 10.6±7.4 ng/mL. The mean prostate volume was 56±25.8 mL among the current study patients.

Complete cell count was performed in all patients one day before surgery. Mean WBC count was 7303±1498/μL. Mean±SD percentage of neutrophil was 60.7%±8.01%, lymphocytes 31.9%±8%, eosinophils 4%±1.98%, and monocytes in 3.3%±2.42%, but

there was no report of basophil.

Results of CRP tests were negative in 68 patients (40.5%) and positive in 100 patients (59. 5%). Patient's urinalysis was also examined and it was observed that 113 (67.3%) patients had hematuria (RBC more than 3) and 124 (73.8%) had pyuria; although in no sample bacteria was reported more than 10, all urine cultures were negative.

Pathologic finding

Among the 168 patients undergoing the biopsy, the pathology reports were BPH in 100 patients (59.5%), adenocarcinoma in 59 (35.1%), ASAP in six (3.6%) and active prostatitis in three (1.8. Gleason scorings are shown in Table 1).

Correlations

It was observed that neutrophil counts and neutrophil percentage were not different among the groups with different pathologies. After that the pathologies were divided into two benign and malignant groups and previous findings were confirmed, Figure 1 and 4.

NLR was in contrast with GS (P >0.05).

Urinalysis and CRP test had no difference in different cell counts (P >0.05). In comparison to biopsy findings, none of the cell counts (absolute or percent) had suitable specificity and sensitivity (P >0.05).

In multivariate analysis to predict malignancy, only age (B=0.1, S. E=0.04, EXP [B] =1.1 and sig=0.00) and PSA level (B=0.1, S. E=0.04, EXP [B] =1.1 and sig=0.00) were significant.

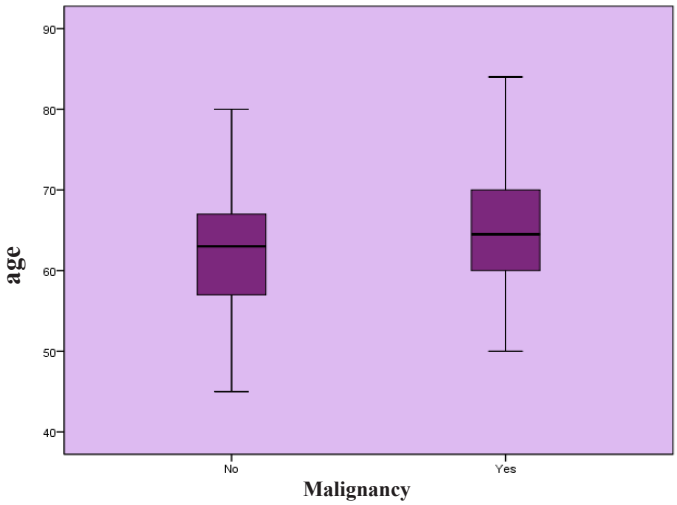

Figure 1. Mean Age of Patients in Different Pathology Groups

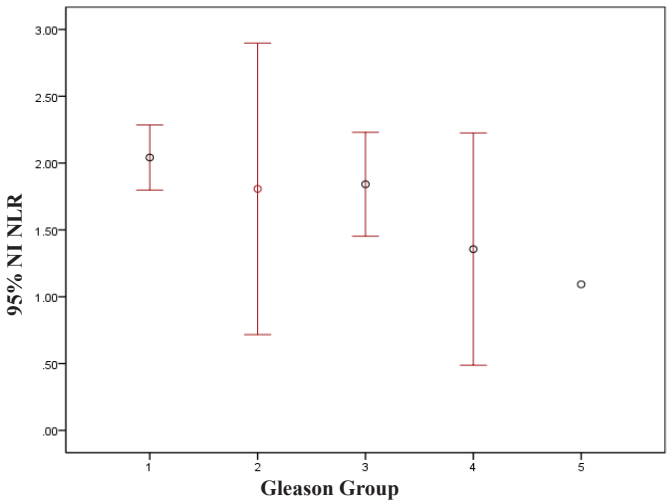

Figure 2. Gleason scoring in patients diagnosed with adenocarcinoma in five distinct grade groups based on the modified Gleason score groups. Grade group 1 = Gleason score ≤6, grade group 2 = Gleason score 3 + 4 = 7, grade group 3 = Gleason score 4 + 3 = 7, grade group 4 = Gleason score 8, grade group 5 = Gleason scores 9 and 10.

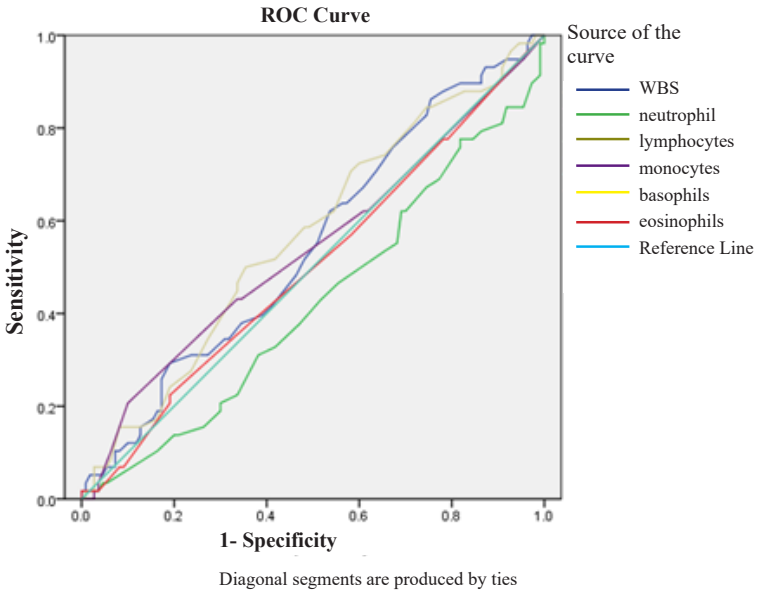

Figure 3. ROC curve shows specificity and sensitivity of blood cell counts to diagnose prostate adenocarcinoma

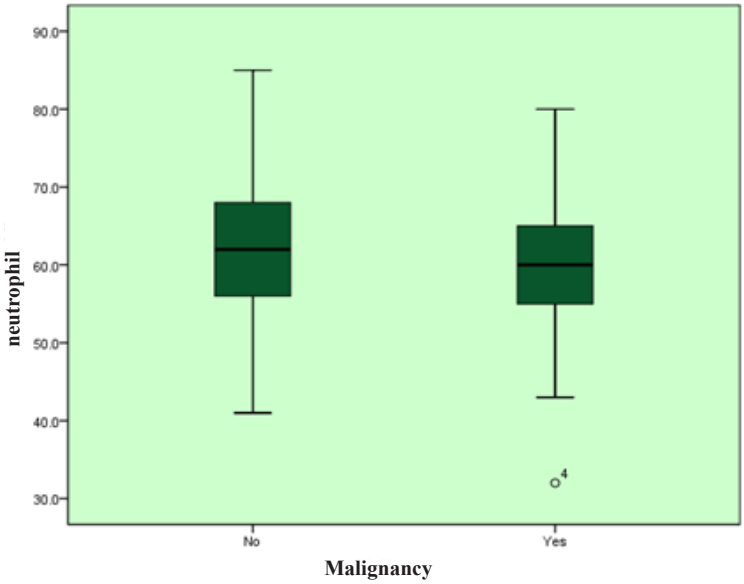

Figure 4. Neutrophill Percentage in Patients With and Without Adenocarcinoma

Discussion

Little data were found about NLR and its prognostic value on histology of prostate biopsies (6-8).

Inflammation's dark side is a dominant power in cancer growth, where it supports and assists tumor growth and metastasis (9). Neutrophils can have an important influence on the tumor microenvironment via their specific characters to modify tumor cell proliferation, angiogenesis, and metastasis, and due to that some researchers explored tumor-associated neutrophils as a means of antitumor therapy (10).

No relationship was observed between hematologic, inflammatory, and laboratory findings of the blood count and histology of prostate biopsy. Fujita et al., (11) showed an elevated neutrophil count that can be an indicator of good prostate biopsy, unlike finding was proposed by Kawahara (12). Although some researchers did not find any differences between NLR and prostate biopsy (6), similar to the results of the current study, data discrepancy may be due to different methods and lack of sufficient data; especially data about NLR were inconsistent, blood sampling was different with respect to time and antibiotic thera-

py (13, 14), also most of studies investigated NLR on survival (15) and some researchers evaluated its impact on specific PCA groups such as metastatic castration resistant prostate carcinoma (mCRPC) (16).

No association was observed between NLR and PSA. Yuksel (17) also did not find any relationships between PSA and NLR; pretreatment NLR was observed in the majority of studies unrelated to PSA (6, 7, 13), but there was a relationship after treatment (14). Maeda et al., (12) reported that NLR, with or without combination with F/T PSA ratio, may function as a new biomarker to predict prostate cancer in males undergoing prostate needle biopsy. Although some researchers believe that NLR is related to PSA (6, 18), Kawahara (13) reported no significant relationship between NLR and PSA lower than 20 ng/dL , but Sümbül reported that NLR was effective to predict the PSA response in chemotherapy.

As already mentioned, theoretically, systemic inflammation might have an effect on the development and progression of cancer, raised CRP (18), but the current study did not observe such a relationship. McDonald et al. (18), reported that serum CRP to PSA association was not significant after age and multivariable adjustments, similar to the current study findings.

In contrast to the current study findings, Gokce (6) revealed that higher GS was associated with higher NLR. Lee et al., (19) reported that high NLR was significantly related to unfavorable clinicopathological outcomes. Further studies are required to clarify the correlation between NLR and GS.

Gu et al. (15), in a comprehensive meta-analysis, revealed that increased NLR could predict poor overall survival, progression-free survival, and recurrence-free survival. In another recently conducted meta-analysis, increased NLR had a strong relationship with poorer prognosis metastatic castration-resistant prostate cancer (21).

In conclusion, since the results of the current study showed no significant relationship between NLR and PSA, CRP or the pathologic results of the prostate TRUS biopsy, the physicians should reconsider using NLR as a decision making parameter to diagnose and approach the patients suspected to prostate cancer, BPH or inflammatory processes such as prostatitis. Prescription of any kind of medications or antibiotic therapies before prostate biopsy should not be relied on the neutrophil count or the NLR index only.

Weakness: It seems to be crucial to evaluate long term prognostic value of blood cell count.

Conflict of interest

The authors declare that there was no conflict of interest.

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How to Cite This Article

Khosrovpanah I, Heidari bateni Z, Rostami S, Khosrovpanah D, Teimoori M. Prognostic value of neutrophil to lymphocyte ratio on pathologic findings of Transrectal ultrasonography guided biopsy of prostate. Iranian Journal of Pathology, 2018; 13(3): 333-339