International Journal of Medical Science and Clinical Invention 5(07): 3928-3930, 2018
DOI:10.18535/ijmsci/v5i7.08 **ICV 2016: 77.2**
e-ISSN:2348-991X, p-ISSN: 2454-9576

Research Article

Correlation between Pretreatment Platelet to Lymphocyte Ratio and Pretreatment Neutrophil to Lymphocyte Ratio with Prognosis in Prostate Cancer Patient in H. Adam Malik General Hospital Medan

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Abstract:

Introduction: Prostate cancer is one of the medical problems in male population, and is the second most common cancer. According to statistics, the prevalence of prostate cancer in Europe is 214 / 100,000 and the number of cases diagnosed each year is 2.6 million. High incidence of prostate cancer in Indonesia, made it necessary to find an examination that can be used widely in major health centers with good sensitivity and specificity. Platelet and lymphocyte counts are routinely performed in most clinical laboratories around the world, therefore we evaluate whether pretreatment PLR and NLR can predict prognosis for prostate cancer patients.

Methods: This study was conducted by using cross sectional analytical method in Urology Department of Urology Division of H. Adam Malik General Hospital Medan from 2012 until 2017. We analyzed 70 samples that met inclusion and exclusion criteria with Spearman correlation test in SPSS Statistic 23.

Results: From 70 samples that has been analyzed, we found that 42 samples (60%) subjects were diagnosed with prostate adenocarcinoma and the other 40% with prostatic hyperplasia. Median pretreatment PLR score is 175.2 (75-553.8) and median score for pretreatment NLR 3.4 (1.4-20.5). Both pretreatment PLR and NLR had a weak negative correlation with Karnofsky score (R = -0.257, p = 0.032 and R = -0.247, p = 0.039, respectively)

Conclusion: The higher number of pretreatment PLR score correlate to worse prognosis of prostate cancer patients and the higher number of pretreatment NLR score, correlate to worse prognosis of prostate cancer patients.

Keywords: Platelet to Lymphocyte Ratio, Neutrophil to Lymphocyte Ratio, Prostate Cancer, Karnofsky Score, Prognostic Factor.

Introduction

Prostate cancer is one of the medical problems in male population, and is the second most common cancer. Prostate cancer causes number 5 on cancer-related deaths in men worldwide. According to statistics, the prevalence of prostate cancer in Europe is 214 / 100,000 and the number of cases diagnosed each year is 2.6 million. From the data of the Indonesian Society of Urologic Oncology (ISUO) 2011 during the period 2006-2010 there were 971 patients with prostate cancer. The mean age was 68.3 years, the highest among age group 70-79 years was 37.6%. Diagnostic modalities were used primarily biopsy of 563 cases (57.9%). High incidence of prostate cancer in Indonesia, made it necessary to find an examination that can be used widely in major health centers with good sensitivity and specificity so that it can be used as a parameter in assessing prognosis prostate cancer.

Neutrophil-to-lymphocyte ratio (NLR) is the most commonly used method because it is easily accessible. Recent evidence indicates that NLR is associated with poor life expectancy in patients with prostate cancer (PCa). Similarly with NLR, Platelet-to-Lymphocyte (PLR) is a way that can be used to predict the prognosis of patients with prostate cancer, but is still rarely used worldwide. (Cao J, Zhu X, 2016) More and more evidence suggests that inflammation may have a major role in tumorogenesis and PCa development. A low number of serum neutrophils predicts a positive prostate biopsy. NLR appear to represent independent prognostic markers in patients with PCa. Similarly PLR is also a parameter based on systemic inflammation. A number of studies have revealed high pretreatment PLR independently predicting poor prognosis in patients with tumors including stomach cancer, pancreatic cancer, ovarian cancer, colorectal cancer, lung cancer, hepatocellular carcinoma, kidney cancer, esophageal cancer. Yuksel OH et al and Kaynar M et al. reported that PLR is commonly used to distinguish benign prostatic hyperplasia and prostate cancer, to support its diagnostic value. However, whether pretreatment PLR and NLR play an

important role in PCa prognosis has not been reported. Platelet and lymphocyte counts are routinely performed in most clinical laboratories around the world, therefore we evaluate whether pretreatment PLR and NLR can predict prognosis for prostate cancer patients.

Methods

This research was conducted by using cross sectional analytical method in Urology Department of Urology Division of H. Adam Malik General Hospital Medan with data taken from medical record of outpatient department of urology of H. Adam Malik General Hospital Medan from 2012 until 2017.
Target population is Patients with prostate cancer. Accessible populations are outpatients who have been diagnosed with prostate cancer in H. Adam Malik General Hospital from 2012 until 2017. The sample of the research is a patient with a diagnosis of prostate cancer that has been done by histopathologic examination through simple random sampling technique that has met the criteria of inclusion and exclusion. Inclusion criteria are all patients with prostate cancer who have been diagnosed histopathologically in H. Adam Malik General Hospital Medan, with complete medical record data, and approve with informed consent by the patient. Exclusion criteria are incomplete medical record results (patient data in the form of address and telephone number, laboratory results of routine blood), patients with metabolic disorders such as Type 2 diabetes mellitus and haematological disorders and infections.

Results

In this study, the normality tests were performed using Kolmogorov-Smirnov (KS) test for numerical data. The results of the KS test are listed in Table 1. It was found that prostate-specific antigen (PSA), haemoglobin, leukocyte, absolute platelet count, absolute lymphocyte count, absolute neutrophil count, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR), all of which have a value of $p < 0.05$, so all the numerical variables in this study do not meet the normality assumptions, thus we use Spearman test to find the correlations between variables.

Variable	p value
PSA	< 0.001
Haemoglobin	0.049
Leukocyte	0.001
Absolute platelet count	0.029
Absolute lymphocyte count	0.041
Absolute neutrophil count	0.011
PLR	< 0.001
NLR	< 0.001
Karnofsky Score	< 0.001

Table1. Kolmogorov-Smirnov (KS) Test Results for Numerical Data

PSA = *prostate-specific antigen*, PLR = *platelet-to-lymphocyte ratio*, NLR = *neutrophil-to-lymphocyte ratio*

In this study, 42 (60%) subjects were diagnosed with prostate adenocarcinoma. The characteristics of the subject are listed in Table 2.

	N	%
Anatomical Pathology Results		
• Prostate Hyperplasia	28	40%
• Prostate Adenocarcinoma	42	60%
PSA	15 (0.8-436.7)[a]	
Haemoglobin	13.3 (8.8-15.9)[a]	
Leukocyte	7.8 (1.1-21.3)[a]	
Absolute platelet count	342 (97-642)[a]	
Absolute lymphocyte count	2 (0.5-46)[a]	
Absolute neutrophil count	7.5 (2.8-19.1)[a]	
PLR	175.2 (75-553.8)[a]	
NLR	3.4 (1.4-20.5)[a]	
Karnofsky Score	20 (0-100)[a]	
Mortality	12	17.1%

Table 2. Characteristics of the Subjects

*The abnormally distributed numerical data is shown in median (minimum-maximum)

PSA = *prostate-specific antigen*, PLR = *platelet-to-lymhocyte ratio*, NLR = *neutrophil-to-lymphocyte ratio*

To know the correlation between pretreatment PLR and Karnofsky score as well as pretreatment NLR and Karnofsky score, Spearman correlation test was performed. It was found that both pretreatment PLR and NLR had a weak negative correlation with Karnofsky score ($R = -0.257$, $p = 0.032$ and $R = -0.247$, $p = 0.039$, respectively) The Spearman correlation test results are shown in Table 3.

	Correlation Coefficient (R)	p value
Pretreatment PLR to Karnofsky score	-0.257	0.032
Pretreatment NLR to Karnofsky score	-0.247	0.039

Table 3. Spearman Correlation Test Results

Discussion

Platelets and lymphocyte count are blood-based parameters that are measured regularly. Similarly with NLR, PLR is a parameter based on systemic inflammation. A number of studies have reported that independently, PLR predicts poor prognosis in patients with tumors, including gastric cancer, pancreatic cancer, ovarian cancer, colorectal cancer, non-small cell lung cancer, hepatocellular carcinoma, renal cell carisnoma, esophageal cancer. Yuksel et al and Kaynar et al reported that PLR can differentiate benign prostatic hyperplasia and prostate cancer (Yuksel et al, 2015; Kaynar et al, 2015). Langsenlehner reported a significant association between PLR and prognosis in patients with prostate cancer undergoing radiation therapy. (Langsenlehner et al., 2015) In this study, found weak negative correlation of PLR to Karnofsky score, with value P <0.005, Correlation Coefficient (R = -0.257). This indicates that PLR is a predictor of mild prognosis. In this study, we also found that the higher the NLR level, the worse the prognosis of prostate cancer patients (P <0.005, R = -0.247). This is similar to previous studies. Meta-analysis of 22 studies involving 18,092 cases found that the increase in NLR was a mild risk factor for biochemical recurrence (BCR) in patients with prostate carcinoma after radical prostatectomy. It was found that the increase in NLR was a strong predictor of predicted PSA response (PRPSA) in patients with metastatic castration-resistant prostate cancer (mCRPC). Increased NLR predicts poorer OS, PFS, and recurrence-free survival (RFS) (Cao et al., 2016). Gu et al., In his meta-analysis involving 15 prospective studies in 16,266 patients, also found that the increase in NLR was associated with worse OS and PFS / RFS in prostate cancer patients (Gu et al., 2015). Meanwhile, meta-analysis by Yin et al. discovered that NLR increase is related to OS on mCRPC but not on NLC. However, the meta-analysis performed by Cao et al has more evidence with lower heterogeneity (Yin et al., 2015).

Conclusion

In this study, we found that the higher number of pretreatment PLR score correlate to worse prognosis of prostate cancer patients. The higher number of pretreatment NLR score, correlate to worse prognosis of prostate cancer patients.

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