RESEARCH ARTICLE

Evaluation of Platelet Indices in Lung Cancer Patients

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Abstract

Background: In this study, we aimed to determine platelet indices such as platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), Plateletcrit (PCT) platelet count (PLT) in lung cancer cases, and evaluate any relationships between these parameters and stage or histologic types. Materials and Methods: This retrospective study covered 44 lung cancer patients and 47 healthy subjects. Platelet indices including PLT, PCT, MPV, PDW were estimated and compared with normal subjects. The results were evaluated statistically. Results: The PDW value was significantly higher in the cancer group compared to the control group; however, the values for PCT and MPV were lower. Conclusions: We suggest potential use of platelet indices in diagnosis of lung cancer.

Keywords: Lung cancer - mean platelet volume - platelet distrubition width - plateletcrit

Asian Pac J Cancer Prev, **16 (17)**, 7599-7602

Introduction

Lung cancer is the most common type of cancer that is cause of death worldwide. The incidence of lung cancer is increasing by the time. This disease can be diagnosed in the middle or later stages due to the lack of specific symptoms of the disease (Zhu et al., 2014). It may be in different histological types such as small cell lung cancer, squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma and large cell anaplastic carcinoma. Approximately 85% of the causes of lung cancer is smoking followed by genetic factors, radon gas, asbestos and air pollution exposure (Shackelford et al., 2014). Although diagnostic applications of lung cancer, treatment options and surgical approaches are improved in recent years, the 5-year survival rate varies around 15%. Therefore, it is very important to be searching new markers to enhance the patient's life and choose the best treatment (Yang et al., 2014).

New hematology analyzers have enabled the evaluation of the parameters that can be used clinically in addition to be used as platelet count (PLT). Parameters related to platelet size reflect platelet activity and named as platelet indices. Mean platelet volume (MPV), platelet distribution width (PDW) and plateletcrit (PCT) are among these platelets indices. MPV shows the average size of platelets in the bloodstream, but it does not reflect changes in platelet size observed microscopically. PDW is calculated as the coefficient of variation in mean platelet volume. High PDW values show that the change in mean platelet volume is more than usual. Some automated hematology analyzers use the number of MPV and platelets in order to calculate PCT used to evaluate the mass of platelet which is the analog of the hematocrit (HCT) that is the indicator of red cell mass. Platelet plaque formation seems to be largely associated with the mass of platelets rather than PLT. PCT can provide additional information for a better evaluation of primary hemostasis in the presence of high MPV values in particular (Mahdavi-Zafarghandi et al., 2014; Schwartz et al., 2014).

In recent years, the number of studies suggesting that PLT and their indices can be used as inflammatory markers in cancer cases in addition to cardiovascular, cerebrovascular, inflammatory and thromboembolic diseases is increasing by the time (Kisacik et al., 2008; Muscari et al., 2009; Yüksel et al., 2009; Berger et al., 2010; Braekkan et al., 2010; Chu et al., 2010) The high reproducibility, low cost, and high applicability of these parameters make it suitable in terms of usability. In this study, we aimed to determine the platelet indices such as MPV, PDW, PCT and PLT in lung cancer patients and evaluate the relationship between these parameters and stage or histological types.

Materials and Methods

Patients

In the retrospective cross-sectional study, blood analyses obtained in the preoperative period from 44 patients received surgical treatment after being diagnosed with lung cancer in the Thoracic Surgery Clinic of Selcuk University Faculty of Medicine between July 2013 and July 2014. Complete blood count analysis results of 47 healthy people admitted to the clinic for routine checks

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were used as the control group. The age distribution of the patient and control groups were similar. Patients were distributed based on their histologic type, stage and metastasis status. We have grouped into three groups in terms of histological types squamous cell carcinoma (SCCa) (n=25), adenocarcinoma (n=10) and others, including small cell carcinoma large cell neuroendocrine carcinoma, cell neuroendocrine ca, carcinoid tumour, pleomorphic carcinoma, (n=9) respectively. According to pathological staging, most of the patients are in the 1st stage (n=28) while the number of patients in other stages are 9 (II), 3 (III) and 4 (IV), respectively. Therefore, we evaluated the patients in two groups as follows; in early stage (stage I) and middle and late stages (stage II, III and IV). Patients were also evaluated based on whether they receive adjuvant chemotherapy and radiotherapy and they smoke or don't smoke. The demographic data of patient and control groups are summarized in Table 1.

Statistical analysis

Data were statistically analyzed using Statistical Package for Social Sciences version 15.0 (SPSS Inc, Chicago, IL, USA). The distribution analyses of demographic data and complete blood count parameters of both groups are conducted by Kolmogorow-Smirnov test. Student t- test Mann-Whitney U test were used to evaluate differences between the groups. The significance level of tests was accepted as $p<0.05$.

Results

PLT and PDW were significantly higer in cancer group compared to control group; however, the values of PCT and MPV were lower (P=0.04, 0.001, 0.02, 0.001, respectively) (Table 2). PLT and PCT values of the patients with metastasis were higher compared to the patients without metastases (P=0.01, 0.02, respectively) (Table 3). When early stage patients and middle and later stage patients were compared in accordance with histological types, no difference was found in terms of their platelet indices. Furthermore, when patients were grouped as patients received/did not receive adjuvant chemotherapy and radiotherapy and smokers/non-smokers, no difference was found between groups in terms of the PLT and indices.

Table 1. Characteristics of the Patient and Control Groups

Characteristics	Patients (n= 44)	Control (n=47)
Age,years (mean ± SD)	59.28±8.47	57.12±12.89
Sex		
Female	8	18
Male	36	29
Histological diagnosis		
Squamous cell carcinoma	25	
Adenocarcinoma	10	
Others	9	
Initial clinical stage		
Stage I	28	
Stage II, III,IV	16	
Adjuvant chemotherapy (Yes/No)	23/21	
Adjuvant radiotherapy (Yes/No)	6/38	
Smoking history		
Never smoked	18	
Past or current smoker	27	

Table 2. Complete Blood Count Parameters of Patient and Control Groups

Parameters	Patients (Mean±SD)	Control	p value
N	44	47	
RBC(10^{12}/L)	4.70±0.51	5.00±0.53	0.009
WBC(10^9/L)	8.95±1.29	7.33±1.63	0.195
MCV(fL)	87.48±6.75	85.23±5.73	0.012
MCH(pg)	29.49±.53	29.26±2.55	0.569
MCHC(g/dL)	33.0±4.61	34.06±1.28	0.037
RDW(%)	15.88±1.83	14.27±3.00	0.001
NEU(10^9/L)	5.88±3.02	4.68±1.29	0.153
LYM(10^9/L)	7.04±31.62	2.68±2.94	0.851
PLT (10^9/L)	283.04±100	241.14±80.41	0.04
MPV (fL)	7.38±1.24	9.92±1.03	0.001
PDW (%)	17.67±0.94	11.07±1.92	0.001
PCT (%)	0.2 ±0.06	0.23±0.07	0.02

Table 3. Platelet Indices in Patients With and Without Metastasis

Parameters	Metastasis (+) (Mean±SD)	Metastasis (-)	p value
N	5	39	
PLT (10^9/L)	414.4±139.06	266.2±83.02	0.01
MPV (fL)	6.87±0.88	7.45±1.28	0.386
PDW (%)	17.4±0.48	17.39±0.98	0.27
PCT (%)	0.27±0.07	0.19±0.06	0.021

Discussion

In our study, we have evaluated PLT and MPV, PDW and PCT in patients with lung cancer and healthy control group. While PLT and PDW were found significantly higher in the patient group with lung cancer compared to control group, the values of MPV and PCT were found to be lower.

Although there are several studies suggesting that PLT increases in various organ cancers compared to control groups, there are also some other studies suggesting that there is no change in PLT. Although it has been stated that PLT increases in patients with non- small cell lung cancer (NSCLC) and epithelial ovarian cancer, no change is observed in PLT in patients with malignant adnexal mass, breast cancer and colon cancer compared to control group (Inagaki et al., 2014; Li et al., 2014; Ma et al., 2014; Ozaksit et al., 2014; Okuturlar et al., 2015). Although genetic factors are known to be the basic mechanisms underlying in cancer development, it has been stated that host inflammatory response has a very important role in carcinogenesis. Local tumor-associated inflammation shows systemic inflammatory response that can be easily identified in the preoperative period. In this period, release of inflammatory cytokines and acute phase reactants increases. Proinflammatory cytokines lead

proliferation and megakaryocytes convert into platelets in the myeloid of immune and hematopoietic cells (Coupland et al., 2014). Platelets also play an important role in synthesis and release of vascular endothelial growth factors that is involved in tumor angiogenesis in addition to inflammation in tumor pathogenesis (Tuncel et al., 2014). Activated platelets play a a key role in the occurrence of thrombotic events through the activation of the coagulation cascade (Li et al., 2014). In many cancer types, coagulation and fibrinolysis systems are being activated and tumor metastasis is associated with invasion and poor prognosis (Okuturlar et al., 2015). In this study, PLT is found to be significantly decreased compared to control group.

MPV is the geometric mean calculated from the logarithmic transformation of distribution curve of platelet volume. Platelet is an index indicating the width. Under normal circumstances, there is an inverse relationship between the number and volume of platelet in order to maintain a constant mass of circulating platelets. When PLT is decreased, megakaryocytes in the bone marrow is stimulated by thrombopoietin and their nucleuses transform into hyper lobul which has a high DNA content. These megakaryocytes stimulated become larger platelets (Alsweedan et al., 2008)). According to a study conducted with patients diagnosed with lung cancer, no difference was found between patients and healthy control groups in terms of MPV values (Kemal et al., 2014). On the other hand, the value of MPV is reported to be reduced in NSCLC which supports our conclusion (Karagoz et al., 2009; Inagaki et al., 2014). However, in our study, we have seen that the value of MPV is lower compared to the control group. There are two possible reasons of this lower value. First, since larger platelets are more active and more responsive against endogenous and exogenous stimuli compared to smaller platelets, they may cause consumption of these cells (Inagaki et al., 2014; Li et al., 2014). The other reason might be that small platelets may be more prominent in circulation depending on destruction and sequestration of platelets in the active inflammation (Ceylan et al., 2015). MPV can be a marker that can be used in the differential diagnosis of thrombocytopenia and to determine whether solid tumors have metastasis on bone marrow (Aksoy et al., 2008; Chandra et al., 2010). In our study, one of the reasons why MPV values are low may be that most of the patients included in the study have early-stage lung cancer without metastasis. Increased value of MPV in patients diagnosed with gastric, endometrial, colon and epithelial ovarian cancer is in conflict with our results (Oge et al., 2013; Kılıncalp et al., 2014; Li et al., 2014; Ma et al., 2014). Variability of MPV values in cancer patients may be due to different study methods used and effects of EDTA on the results (Dundar et al., 2008). In addition, since one of the factors affecting the value of MPV is the time of analysis, the value of MPV can vary because this variable is not taken into account in retrospective studies (Vagdatli et al., 2010).

PDW is the standard deviation of the logarithmic transformation of platelets. The increase of PDW shows that abnormal large and small platelets are in the circulation and it is an index give an idea idea about the viability of platelets to be used in transfusions. PDW is a more useful parameter compared to MPV in making the distinction of thrombocytopenia depending on the destruction increase rather than thrombocytopenia depending on production shortage (Alsweedan et al., 2008). In normal individuals, PDW is linearly related to MPV (Leal-Santos et al., 2013). In the literature, in studies conducted with cancer patients, MPV and PDW is not found to be parallel with each other (Okuturlar et al., 2015; Ozaksit et al., 2015). This conclusion is consistent with our results. Furthermore, we have seen that PDW is evaluated simultaneously with other inflammatory parameters rather than its direct relationship with various types of cancer. In the literature, there are different results in PDW. In the study of Ma et al., in which platelet indices in patients diagnosed with epithelial ovarian cancer and healthy control group are discussed, the value of RDW is increased in the patient group which is consistent with the value of PDW we have obtained. Although no difference was found between patients with neoplastic adnexal mass and breast cancer and control group in terms of PDW values, this value was found to be lower in patients diagnosed with NSCLC (Inagaki et al., 2014; Ma et al., 2014; Ozaksit et al., 2014; Okuturlar et al., 2015).

Another parameter- PCT, which is a measure of platelet mass, is calculated using PLT and MPV. In intensive care units, PCT values, which are obtained by multiplying PLT and MPV, are used rather than using only the value of platelets during platelet transfusions. There are some guidelines that are determined by this calculation. The risk of bleeding is increased as the value of PCT increases (Gerday et al., 2009; Estcourt et al., 2010). Information about how the PCT changed during the course of the disease is very limited. Therefore, it is often neglected in clinical practice and very few studies reported this issue in the biomedical literature. Changes in the PCT have been reported in a small number of inflammatory diseases and cancer patients (Leal-Santos et al., 2013). While Ozaksit et al. (2015)have stated that there is no difference between two groups with malignant and benign adnexal masses and control group in terms of PCT values, Xuegong et al. (2008) have determined that the value of PCT is higher in patients with epithelial ovarian cancer compared to the healthy control group (Ma et al., 2014; Ozaksit et al., 2015). In our study, we have found the value of PCT lower in the patient group compared to control group.

We have seen that there are different results PLT and indices of platelets when they are evaluated according to stage, histological type and metastasis status in various types of cancer. While PLT in patients with breast cancer is found to be lower in patients with metastasis, MPV and PDW didn't change in the tumor stage (Okuturlar et al., 2015). In patients diagnosed with lung cancer, it has been found that MPV is not changed depending on tumor stage and histologic types (Kemal et al., 2014). In patients diagnosed with colon cancer, although there is no difference between the groups with metastasis and without metastasis in terms of MPV, it has been found to be lower in I-II stages compared to III-IV stages in the early stage cancer (Li et al., 2014). In our study, while PLT is found to be higher in patients with metastasis compared

to the patients without metastasis, there was no difference between the groups in terms of MPV and PDW values. In addition, in our study, we have observed PLT, MPV, PDW and PCT didn't change related with tumor stage, histological type and metastasis status.

Platelets are involved in the pathogenesis of inflammation besides their their role in coagulation system. It has been suggested that the number and indices of platelets can be used as new markers of inflammation in these cancer types. Our results regarding platelet indices are consistent with this relationship.

We suggest that the usability of PLT and indices in early diagnosis of lung cancer, determination of recurrence and in the follow-up of treatment should be evaluated by further studies to be conducted on larger populations diagnosed with lung cancer.

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