Res. Oncol.
Vol. 12, No. 1, Jun. 2016:15-19

Original article

The relation between mean platelet volume/platelet count ratio and prognostic factors in patients with advanced non-small cell lung cancer

Amal R. Ibrahim, Ola N. Abdel Fattah

Department of Clinical Oncology, Faculty of Medicine, Assiut University, Assiut, Egypt

Background: Identifying simple and reliable prognostic indicators in non-small cell lung cancer (NSCLC) is important to optimize its management. The mean platelet volume/platelet count (MPV/PC) ratio may be of prognostic value in some clinical conditions including NSCLC.
Aim: To investigate the relationship between MPV/PC ratio and some important prognostic factors in Egyptian NSCLC patients.
Methods: Retrospective study that included 69 patients with stage III/IV NSCLC in the period from January 2010 to December 2012. The complete blood picture done before starting treatment was the one considered for the calculation of MPV/PC. The relation between MPV/PC ratio and patients and disease characteristics was studied.
Results: More advanced stage was associated with lower average MPV/PC ratio. The average MPV/PC ratio was 0.45963 (95%CI: 0.38829- 0.53098) in patients with stage IIIA, 0.33873 (95%CI: 0.2854-0.39208) in stage IIIB and 0.32752 (95%CI: 0.28642- 0.36862) in stage IV (p=0.015).
Similarly, higher Eastern Cooperative Oncology Group performance status score was associated with lower MPV/PC ratio. The average MPV/PC ratio was 0.40949 (95%CI: 0.34959 – 0.46939) in patients with ECOG 1, 0.36369 (95%CI: 0.31009- 0.41724) in ECOG 2 and 0.28378 (95%CI: 0.24898 -0.31857) in ECOG 3 (p=0.004). Older patients had a significantly lower MPV/PC ratio (p=0.043).
Conclusion: Low MPV/PC is associated with poor prognostic factors in NSCLC such as advanced stage and poor performance status. Future clinical studies to evaluate the prognostic value of MPV/PC ration in NSCLC are warranted.

Key words: "Non-small cell lung cancer, Prognosis, Mean platelet volume/platelet count (MPV/PC) ratio".

Corresponding Author: Amal R Ibrahim, **E-mail:** amal3774rayan@gmail.com, Tel: +20 1022454482

Received: 19-Dec-2015, Accepted: 11-Jan-2016

Original article

INTRODUCTION

Lung cancer is highly lethal tumor. The 5-year relative survival rate varies markedly, depending on how advanced the disease is at diagnosis[1], as follows: 49% for local disease, 16% for regional disease, 2% for distant stage disease.

Mean platelet volume (MPV) is a platelet volume index[2]. Classically, MPV was recognized gnized as a hallmark of platelet activation. There fore MPV is related to various thromboembolic disorders. Besides, MPV is the most commonly used measure of platelet size and is a potential marker of platelet reactivity. Noteworthy, MPV is typically in the range of 5 -15 femtoliters. Recent studies revealed that MPV/PC ratio can predict long term mortality in patients with ischemic cardiovascular diseases[3].

These indices were also associated with the pathophysiologic characteristics of various disorders including malignant tumors[4], the prognostic impact of "platelet count" Approximately one third of patients present with locally advanced non metastatic disease, many of whom are surgically unresectable due to the extent of disease or medically inoperable because of pulmonary and/or other co-morbidities.

Thrombocytosis was recognized as unfavorable predictive factor for overall survival. In a Japanese study, MPV/PC ratio was closely associated with survival in patients with advanced NSCLC with cutoff value of 0.408730 (sensitivity of 62.3%, specificity of 74.6%)[6].

The aim of this study was to study the relation between MPV/PC ratio and some prognostic factors in advanced NSCLC patients

METHODS

Patients with advanced NSCLC (stage III, stage IV) were included and their files were retrospectively evaluated during the period from January 2010 to the end of 2012. The clinical stage was assigned based on the 7th edition of TNM classification of lung cancer[7].

We have reviewed all patients' medical records at Clinical Oncology Department, Assuit University Hospital for sex, age, histologic subtype, smoking history, staging and Eastern Cooperative Oncology Group "ECOG" performance status.

The first complete blood pictures of patients before the start of systemic chemotherapy were reviewed for platelet indices; mean platelet volume (MPV) and platelet count, then the ratio was calculated, the cut off value was previously determined to be 0.408730 (sensitivity of 62.3%, specificity of 74.6%)[6].

patients were grouped into two groups above and below the previous cutoff point. The demograghic and clinical characteristics of each group were determined Patients with large cell neuroendocrine carcinoma, previous curative thoracic irradiation were excluded. Also those with previous history of malignancy or elevated C-reactive protein or active infection were excluded. Statistical analysis was performed using the Statistical Package for the Social Sciences, version 14.0 (SPSS Inc, Chicago, Illinois). All statistical tests were two sided and $P<0.05$ was considered significant.

RESULTS

From January, 2010 to December, 2012, a total 69 patients with advanced NSCLC were enrolled.

The clinical characteristics of patients are shown in Table (1).

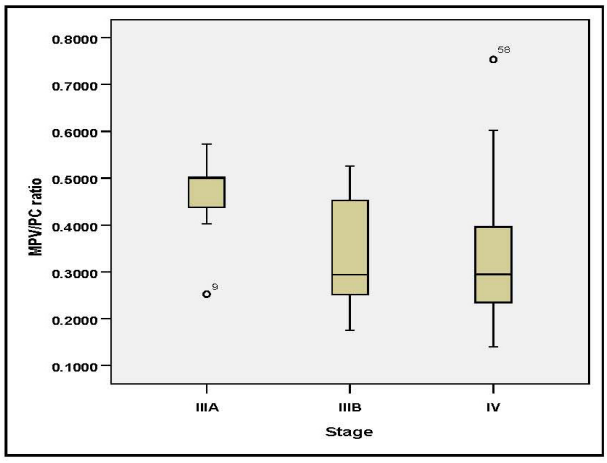

Figure 1: The average MPV/PC ratio according to the stage in patients with advanced NSCLC (p=0.015).

The average MPV/PC ratio for the whole group of patients was 0.348327 (±0.1261) and the median was 0.32157 (range: 0.1403 – 0.7535).

Lower average MPV/PC ratio was associated with more advanced stage (Figure 1).

The average MPV/PC ratio was 0.45963 (95%CI: 0.38829 -0.53098) in patients with stage IIIA, 0.33873 (95%CI: 0.2854 -0.39208) in patients with stage IIIB and 0.32752 (95% CI: 0.28642- 0.36862) in patients with stage IV (p=0.015).

Lower average MPV/PC ratio was associated with higher ECOG performance status score (Figure 2).

The average MPV/PC ratio in patients with ECOG 1 was 0.40949 (95% CI: 0.34959 –0.46939), ECOG 2 was 0.36369 (95% CI: 0.31009- 0.41724) and ECOG 3 was 0.28378 (95% CI: 0.24898- 0.31857) and the difference was highly significant (p=0.004).

Older patients had a significantly lower MPV/PC ratio as shown in Figure 3 (Pearson correlation = -0.245, p=0.043).

Using the cutoff value of 0.40873, patients were divided into two groups. The comparison between the two groups is shown in Table 2.

Patients with an MPV/PC ratio <0.40873 were significantly more likely to be older in age, have a worse performance status and higher stage. There was no significant correlation with sex, smoking history or histologic subtype.

The median follow up duration for patients with an MPV/PC ratio below 0.40873 was much lower than that of patients with a ratio above 0.40873 (5 months [95% CI: 4.27- 5.73] vs. 15 months [95% CI: 12.86- 17.14], respectively).

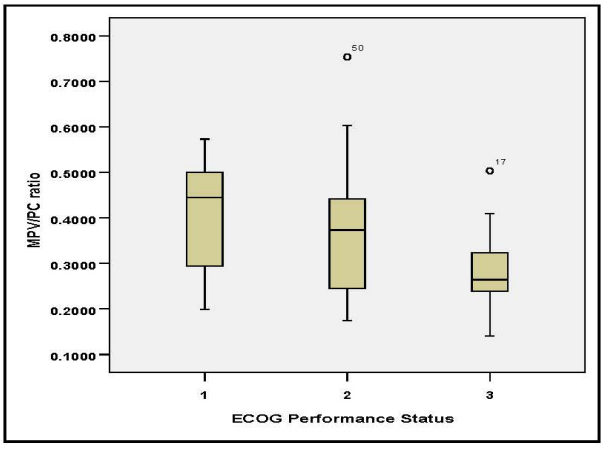

Figure 2: The average MPV/PC ratio according to the ECOG performance status of patients with advanced NSCLC (p=0.004).

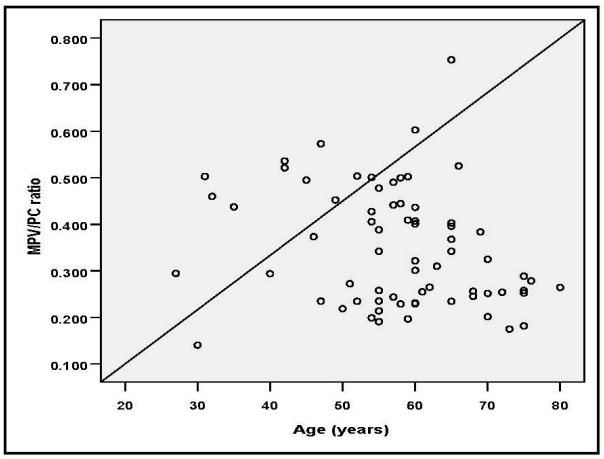

Figure 3: The relation between MPV/PC ratio and age of patients with advanced NSCLC.

Table 1: Patients' characteristics

	N	%
Age in years (median, range)	59 (27-80)	
Sex		
Male	43	62.3
Female	26	37.7
Smoking		
Current	20	29
Past	20	29
Never	29	42
Eastern Cooperative Oncology Group Performance status		
1	17	24.6
2	29	42
3	23	33.3
Histologic subtype		
Adenocarcinoma	40	58
Squamous cell carcinoma	17	24.6
Large cell carcinoma	4	5.8
Mucoepidermoid carcinoma	3	4.3
Broncho-alveolar carcinoma	2	2.9
Adenoic cystic carcinoma	1	1.4
Carcinoma with metaplasia	1	1.4
Mucinous adenocarcinoma	1	1.4
Stage		
IIIA	9	13
IIIB	22	31.9
IV	38	55.1
Number of chemotherapy lines		
0	9	13
1	1	40
2	17	24.6
3	3	4.3

Table 2: Comparison between patients with an MPV/PC ratio above and below a cutoff value of 0.40873

Variable	Patients with MPV/PC ratio < 0.40873	Patients with MPV/PC ratio > 0.40873	*P value*
Age			
<60 years	19 (51.4%)	18 (48.6%)	0.001
≥60 years	28 (87.5%)	4 (12.5%)	
Sex			
Male	28 (65.1%)	15 (34.9%)	0.492
Female	19 (73.1%)	7 (26.9%)	
Smoking			
Current	14 (70%)	6 (30%)	0.642
Previous	12 (60%)	8 (40%)	
Never	21 (72.4%)	8 (27.6%)	
ECOG performance status			
1	7 (41.2%)	10 (58.8%)	0.003
2	19 (65.5%)	10 (34.5%)	
3	21 (91.3%)	2 (8.7%)	
Histologic subtype			
Adenocarcinoma	29 (72.5%)	11 (27.5%)	0.615
Squamous cell carcinoma	11 (64.7%)	6 (35.3%)	
Other	7 (58.3%)	5 (41.7%)	
Stage			
IIIA	2 (22.2%)	7 (77.8%)	0.002
IIIB	14 (63.6%)	8 (36.4%)	
IV	31 (81.6%)	7 (18.4%)	

DISCUSSION

In advanced lung cancer (stage III–IV), there are several options of oncology treatment (including chemotherapy, radiotherapy, targeted therapy) or best supportive care alone[8]. The benefits of any treatment must be balanced with side-effects, which are often considerable.

A fundamental factor influencing treatment decisions in advanced lung cancer is the expected prognosis.t here are no good predictors for the benefit of chemotherapy, however, the prognosis is currently being used to select those who receive chemotherapy. In general, good performance status, female sex, age ≤ 70 years, Hb level > 11 g/dL and normal lactate dehydrogenase levels are associated with improved outcomes in patients with advanced NSCLC[9]. Upon the guidelines for lung cancer treatment, the most established factor for assessing prognosis is performance status. Studies have also linked weight loss in lung cancer to reduced survival[10].

Measures of the systemic inflammatory response are of independent prognostic value in cancer. A combination of the inflammatory markers C-reactive protein and albumin termed the modified Glasgow Prognostic Score (mGPS). The so-called mGPS has been the most extensively studied and validated prognostic scoring tool[11].

Recently, evaluation of the MPV is attracting a great deal of interest. Several reports have shown that an elevation of MPV is closely associated with the severity and prognosis of cerebro- and cardio-vascular disorders[3].

In addition to ischemic cardiovascular disorders, the elevation of MPV has also been reported in malignant tumors. Osada et al showed that the MPV was higher in patients with gastric cancer than in control patients[12].

Cho SY et al demonstrated that MPV and MPV/PC ratio were elevated in patients with hepatocellular carcinoma[4].

In this study; we tried to answer why those with high MPV/PC ratio were associated with better OS in comparison to those with low ratio, and found that the former were associated with better other prognostic factors like age, stage, performance status. Platelets play important role in pathophysiology of tumor angiogenesis by transporting vascular endothelial growth factor (VEGF), which is the target for anti-angiogenic agents[13]. MPV is a parameter of platelet size and can reflect changes in the rate of platelet production. Previous studies have demonstrated that the MPV was higher in patients with gastric cancer than in control patients. Also, MPV/PC ratio differed significantly between patients with hepatocellular carcinoma and controls[4]. Oge et al. showed that MPV was significantly higher in endometrial cancer patients than in the control group[13]. Our data showed statistically significant lower MPV/PC ratios in NSCLC patients with poor prognostic indicators, which may be explained by the increased inflammation and increased platelet activation in the advanced disease.

In the study conducted by Inagaki et al, low MPV/PC ratio was associated with significantly shorter overall survival when compared to the other group (10 months vs. 15 months, respectively; p =0.025) in univariate analysis[6]. Multivariate analysis further confirmed that low MPV/PC is an independent predictor of poor overall survival (p=0.0008)[6].

In the current study, low MPV/PC ratio was significantly associated with poor prognostic factors in NSCLC patients; namely poorer performance status, more advanced disease stage and older age. A key consideration in deciding appropriate treatment in an advanced lung cancer patient is prognosis, however, recent work has demonstrated that approximately 10% of metastatic lung cancer patients receive anti- cancer therapy in the last 30 days of life[14].

Accordingly, accurate assessment of prognosis is needed to inform complex decisions between patients and clinicians. Most important is the urgency for improved survival prediction in metastatic lung cancer.

CONCLUSION

Low MPV/PC ratio was associated significantly with poor prognostic indicators in a group of Egyptian patients with advanced NSCLC. Future studies investigating the correlation between MPV/PC ratio and survival of NSCLC patients with different stages are needed.

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