



Prognostic impact of the mean platelet volume/platelet count ratio in terms of survival in advanced non-small cell lung cancer[☆]



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ABSTRACT

Background: Mean platelet volume (MPV) is a platelet volume index. Classically, MPV was recognized as a hallmark of platelet activation. Recent studies have revealed that the MPV and MPV/platelet count (PC) ratio can predict long-term mortality in patients with ischemic cardio-vascular disease. In addition, these indices were correlated with the pathophysiological characteristics of patients with various disorders, including malignant tumors.

Patients and methods: We retrospectively analyzed various hematological indices of patients with advanced non-small cell lung cancer (NSCLC). The aim of this study was to evaluate the contribution of platelet volume indices to survival in these patients.

Results: A total of 268 patients were enrolled in the study. The median age of the patients was 68 years (range: 31–87 years). We compared various hematological indices between the NSCLC group and an age- and sex-matched comparator group. MPV was significantly decreased in the NSCLC group compared to the comparator group. In contrast, the PC was significantly increased in the NSCLC group. Consequently, the MPV/PC ratio was also decreased in the NSCLC group (0.397 vs. 0.501). In receiver operating characteristics (ROC) curve analysis, the MPV/PC ratio was associated with a sensitivity of 62.3% and a specificity of 74.6% at a cutoff value of 0.408730 (area under the curve [AUC], 0.72492). Univariate analysis revealed that overall survival (OS) was significantly shorter in the group with a low MPV/PC ratio than in the other group (median survival time [MST]: 10.3 months vs. 14.5 months, log-rank, $P=0.0245$). Multivariate analysis confirmed that a low MPV/PC ratio was an independent unfavorable predictive factor for OS (hazard ratio [HR]: 1.668, 95% confidence interval [CI]: 1.235–2.271, $P=0.0008$).

Conclusion: These data clearly demonstrate that the MPV/PC ratio was closely associated with survival in patients with advanced NSCLC.

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1. Introduction

Mean platelet volume (MPV) is a platelet volume index [1]. Classically, MPV was recognized as a hallmark of platelet activation. Larger platelets are more reactive than smaller ones as they can more easily release chemical mediators in response to endogenous or exogenous stimuli [2]. Therefore, MPV was considered to be closely correlated with various thromboembolic disorders. Recent studies revealed that the MPV and MPV/platelet count (PC) ratio can predict long-term mortality in patients with ischemic cardio-vascular disease [3,4]. In addition, these indices were also associated with the pathophysiological characteristics of various

disorders, including malignant tumors [5–8]. The prognostic impact of PC in patients with non-small cell lung cancer (NSCLC) has been extensively discussed [9–11]. Thrombocytosis was recognized as an unfavorable predictive factor for overall survival (OS). However, there has been no direct analysis of the survival impact of platelet indices in patients with NSCLC. In this study, we retrospectively analyzed patients with advanced NSCLC. The aim of this study was to evaluate the contribution of platelet volume indices to survival in advanced NSCLC patients. In this report, we clearly demonstrated the survival impact of the MPV/PC ratio in patients with advanced NSCLC.

2. Patients and methods

2.1. Data collection

The medical records of all patients with NSCLC who had undergone medical examination and received treatment from January 2002 to December 2012 at Kansai Medical University Takii Hospital

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Table 1
Patient characteristics.

Characteristics	Total patients (n = 268)	MVP/PC ratio \leq 0.48730 (n = 166)	MVP/PC ratio $>$ 0.408730 (n = 102)	P-value
Age, years				0.1231
Median (range)	68 (31–87)	67 (32–85)	69 (31–87)	
Sex				0.4142
Female	76 (28.4)	50 (30.1)	26 (25.5)	
Male	192 (71.6)	116 (69.9)	76 (74.5)	
ECOG PS				0.7774
0–2	210 (78.4)	131 (78.9)	79 (77.5)	
3 or 4	58 (21.6)	35 (21.1)	23 (22.5)	
Smoking history				0.6054
Never smoked	74 (27.6)	44 (26.5)	30 (29.4)	
Past or current smoker	194 (72.4)	122 (73.5)	72 (70.6)	
Histological diagnosis				0.2380 ^a
Squamous cell carcinoma	63 (23.5)	43 (25.9)	20 (19.6)	
Adenocarcinoma	195 (72.8)	116 (69.9)	79 (77.5)	
Others	10 (3.7)	7 (4.2)	3 (2.9)	
Initial clinical stage				0.3496
IIIB	15 (5.6)	11 (6.6)	4 (3.9)	
IV	253 (94.4)	155 (93.4)	98 (96.1)	
Systemic chemotherapy				0.2353
None	41 (15.3)	22 (13.3)	19 (18.6)	
\geq 1 regimen	227 (84.7)	144 (86.7)	83 (81.4)	

ECOG, Eastern Cooperative Oncology Group; PS, performance status; EGFR-TKI, epidermal growth factor receptor tyrosine kinase inhibitor; MPV/PC ratio, MPV/platelet count ratio. Percentage is represented in parentheses.

^a Squamous vs. non-squamous.

(Moriguchi-City, Japan) were retrospectively reviewed. Patients were included in this study if they had advanced NSCLC (stage IIIB or IV), regardless of whether they had been treated with systemic chemotherapy. The clinical disease stage was assigned on the basis of the seventh edition of the TNM Classification for Lung Cancer [12,13]. Data on sex, age, smoking history, clinical stage, histological typing of cancer, Eastern Cooperative Oncology Group (ECOG) performance status (PS), and OS were obtained retrospectively from the patients' medical records. Patients who underwent thoracic radiation treatment with curative intent were excluded from the study, as were patients with large cell neuroendocrine carcinoma. The age- and sex-matched comparator group was randomly selected from among patients with chronic obstructive pulmonary disease (COPD) or bronchial asthma who had undergone medical examination in our hospital during the aforementioned period. The case–control ratio was defined as 2:1. Patients with a history of malignant tumor were excluded from the comparator group. Patients with levels of C-reactive protein (CRP) higher than the institutional normal upper limit were also excluded from the comparator group, as were patients with an active infection or inflammation. Laboratory data, including the complete blood count (CBC), were obtained from medical records. The results preceding the initial histological or cytological diagnosis of NSCLC were considered.

This retrospective study was performed in accordance with the Declaration of Helsinki and was approved by the institutional ethics review board (the clinical research board of Kansai Medical University Takii Hospital, institutional ID: 24-33, UMIN-CTR: UMIN000010287).

2.2. Biochemical analysis of blood samples

CBC and various platelet volume indices were measured using ethylenediaminetetraacetic acid (EDTA)-treated blood. An automated blood cell counter was used for these analyses (Sysmex XE-2100, Kobe, Japan). The CRP concentration was measured

using an automatic analyzer (Beckman Coulter AU5400, Miami, FL).

2.3. Statistical analysis

Statistically significant differences between the groups were compared using the chi-square or Student's *t* test. Receiver operating characteristics (ROC) curve analysis was used to estimate an optimal cutoff value for the MPV/PC ratio. OS was defined as the time from initial diagnosis to the time of death from any cause or the date the patient was last known to be alive. Univariate and multivariate analyses of OS were performed using the Kaplan–Meier product-limit method with the log-rank test and the Cox proportional hazards model, respectively. The 95% confidence interval (CI) for the survival rate was calculated using Greenwood's method. To calculate the 95% CI of the median survival time (MST), the Brookmeyer and Crowley method was used. All statistical analyses were conducted using the JMP (version 9.0.2) software program for Windows (SAS Institute Inc, Cary, NC). All statistical tests were two-sided, and $P < 0.05$ was considered to be statistically significant.

3. Results

3.1. Patient characteristics

A total of 268 patients with NSCLC were enrolled in this study. The characteristics of these 268 patients are summarized in Table 1. All the patients were Asian (Japanese, Korean, or Chinese), their median age was 68 years (range: 31–87 years), and they included 76 women and 192 men. One hundred and ninety-four patients had a history of smoking whereas the remaining 74 patients had never smoked. The numbers of patients with squamous cell carcinoma, adenocarcinoma, and other carcinomas were 63, 195, and 10, respectively. The ECOG PS was 0–2 in 210 patients and 3–4 in 58 patients. Fifteen patients had stage IIIB disease, whereas 253 patients had stage IV disease. Two hundred and twenty-seven

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