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Regular Article

Platelet-lymphocyte ratio is a predictor of venous thromboembolism in cancer patients

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ABSTRACT

Venous thromboembolism (VTE) is a common complication and a major cause of morbidity and mortality in patients with cancer. In cancer patients, laboratory parameters that predict venous thromboembolism (VTE) are scarce. Platelet/lymphocyte ratio (PLR), which can be easily calculated from the differential blood count, have been proposed as novel markers predictive of thrombotic events. The aim of this study was to determine whether PLR levels might represent significant prognostic indices in cancer patients with VTE. We retrospectively analyzed the clinical characteristics and laboratory parameters in 76 cancer patients with VTE, among 173 patients pathologically confirmed for cancer between June 2008 and December 2013.Receiving surgical procedure (51.3 VS 33.0%, $p = 0.015$), chemotherapy (51.3 VS 40.2%, $p = 0.013$) and the PLR >260 (32.9 VS 14.4%, $p = 0.004$) were significantly different between the cancer patients with VTE and without VTE. Multiple logistic regression analysis showed that receiving surgical procedure (OR = 1.537, 95%CI = 1.241-1.984, $p = 0.021$), chemotherapy (OR = 1.969, 95%CI = 1.321-2.225, $p = 0.013$) and the PLR >260 (OR = 2.757, 95%CI = 1.655-3.862, $p = 0.025$) were independent predictors of a VTE episode in patients with cancer. The results demonstrate that the PLR at the time of cancer diagnosis could be a useful clinically important, independent risk predictor for VTE in cancer patients.

Introduction

Venous thromboembolism (VTE) which includes deep venous thrombosis (DVT) and pulmonary embolism (PE) is a common complication and a major cause of morbidity and mortality in patients with cancer [1,2]. An increasing number of studies have showed that patients with cancer were at an increased risk of venous thromboembolism (VTE) [3]. Moreover, recent researches showed that VTE was the second leading cause of death in cancer patients [4] and the most common cause of death in the postoperative period [5]. Thus, there is an urgent need for us to identify better biomarkers, especially serum biomarkers to predict VTE, which would help clinicians to adopt preventive and therapeutic strategies for risk patients.

There are published literatures suggesting that the inflammation has a significant role in the pathogenesis of venous thrombosis. Inflammation may interfere with various stages of hemostasis, either through the activation of coagulation or through the inhibition of fibrinolysis and anticoagulant pathways [6]. In addition, it is believed that the cancer related inflammatory condition may change the patient's pro-coagulant system, and eventually result in thrombotic events [7].

In this context, the presence of VTE is likely to represent a non-specific response to cancer-related inflammation. Therefore, markers of inflammation may provide useful information to predict VTE. At present, accumulating evidence demonstrated that increased systemic inflammation is associated with poor cancer-specific survival in a variety of cancers. Recently, an increasing number of studies have focused on the prognostic value of an elevated platelet-to-lymphocyte ratio (PLR) in patients with cancer [8,9]. Although PLR had been widely investigated in terms of their prognostic value on cancer survival outcomes [10,11], there are few literature reporting whether PLR is a predictor of venous thromboembolism in cancer patients. To our knowledge, only one literature reported the clinical value of the PLR at the time of VTE diagnosis, in which Ferroni et al found that PLR can be a predictor for response to anticoagulation and survival [12].

Therefore, we preformed this study aim to investigate the predictive value of PLR for venous thromboembolism in cancer patients.

Methods

Patients

We enrolled 173 patients with primary or relapsing/recurrent solid cancers who were older than 18 years, receiving clinical care in the

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outpatient department setting of the Department of Medical Oncology in Shanghai Tenth People's Hospital of Tongji University, between June 2008 and December 2013. Cases and controls were patients of 18 years or older affected by histology confirmed cancer (metastatic or locally advanced) of the lung, stomach, colon, pancreas, kidney, ovary, breast, prostate, and other genitourinary organs. Cases were cancer patients who had a symptomatic or an asymptomatic VTE diagnosed < 2 months before the inclusion in the study. VTE were diagnosed based on radiological evaluation (computed tomography or Doppler ultrasound) among those patients. Controls were cancer patients without VTE enrolled in the same oncology units of the cases. Controls underwent imaging studies to exclude a VTE. The controls were selected to match the cases by sex, age, and cancer site.

Clinical Data

Baseline patient demographics and clinical characteristics were collected by medical chart review. Cancer stages were obtained at the time of initial diagnosis and anticancer treatment at the time of VTE diagnosis was also reviewed. Peripheral venous blood samples were obtained in all patients at the first day of cancer diagnosis. We used an automatic blood cell analyzer (Bayer Advia 2120) to evaluate the complete and differential blood cell counts. Routine hematology, chemistry and coagulation studies were also tested in all patients. The other biochemical parameters were determined by standard laboratory tests. The PLR was obtained by dividing the total count of platelets by lymphocytes count. The cut-off value for "high versus low" PLR has not been unified currently. Thus, in the present study, the cut-off value for "high versus low" PLR value was defined as previously reported. A PLR >260 was considered elevated according to the published literature [12].

Statistical Analysis

All statistical analyses were conducted by using SPSS 21.0 software. Continuous variables normally distributed were expressed as the means ± standard deviations and compared between the case and control groups using the t test. Continuous variables deviated from the normal distribution were expressed as median and range and compared using non-parametric statistical test. The categorical variables were presented as the number of patients and percentages and compared using the chi-square tests. The multiple logistic regression analysis was conducted to explore the risk factors of VTE. A p-value less than 0.05 was considered significant for all statistical analyses.

Results

We retrospectively analyzed the clinical characteristics, laboratory parameters, and PLR in 76(43.9%) cancer patients with VTE and 97(56.1%) cancer patients without VTE between July 2008 and August 2013.The average age of all the cancer patients was 62.0 ± 8.9 years. The majority of patients were female (54.9%). One hundred and seventy-three patients with solid tumors including gastrointestinal cancer (n = 52) breast cancer (n = 20), lung cancer (n = 58), genitourinary cancer (n = 15), prostate cancer (n = 9) and head-neck cancer (n = 19) were studied. Adenocarcinoma was the most frequent histology (49.7%). The proportion of metastatic cancers was 79.8%. 83 (48.0%) patients received corticosteroids treatment, 71(41.0%) patients underwent a surgical procedure and 84(48.6%) patients received chemotherapy. Baseline clinical characteristics and laboratory parameters between two groups are summarized in Table 1.

According to the analysis made by chi-square test, the distributions of receiving surgical procedure (51.3 VS 33.0%, $p = 0.015$), chemotherapy (51.3 VS 40.2%, $p = 0.013$) and the PLR >260 (32.9 VS 14.4%, $p = 0.004$) were significantly different between the cancer patients with VTE and without VTE.

Table 1
Distribution of cancer patients with VTE (cases) and patients without VTE (controls).

Variables	Total(N = 173)	Cases(n = 76)	Controls(n = 97)	*P*
Age (year, n, %)				
<60	50(28.9)	18(23.7)	32(33.0)	0.404
60-69	58(33.5)	27(35.5)	31(32.0)	
≥70	65(37.6)	31(40.8)	34(35.1)	
Gender (n, %)				
Male	78(45.1)	34(44.7)	44(45.4)	0.935
Female	95(54.9)	42(55.3)	53(54.6)	
Cancer site (n, %)				
Gastrointestinal	52(30.1)	24(31.6)	28(28.9)	0.862
Breast	20(11.6)	9(11.8)	11(11.3)	
Lung	58(33.5)	27(35.5)	31(32.0)	
Genitourinary	15(8.7)	7(9.2)	8(8.3)	
Prostate	9(5.2)	3(4.0)	6(6.2)	
Head-neck	19(11.0)	6(7.9)	13(13.4)	
Cancer stage (n, %)				
Locally advanced	35(20.2)	12(15.8)	23(23.7)	0.198
Metastatic	138(79.8)	64(84.2)	74(76.3)	
Cancer histology (n, %)				
Adenocarcinoma	86(49.7)	41(54.0)	45(46.4)	0.445
Squamous cell carcinoma	11(6.4)	4(5.3)	7(7.2)	
Carcinoma NOS	58(33.5)	26(34.2)	32(33.0)	
Undifferentiated carcinoma	18(10.4)	5(6.6)	13(31.4)	
Corticosteroids (n, %)	83(48.0)	42(55.3)	41(42.3)	0.091
Surgery (n, %)	71(41.0)	39(51.3)	32(33.0)	**0.015***
Chemotherapy (n, %)	84(48.6)	45(59.2)	39(40.2)	**0.013***
Hemoglobin(g/dL)	14.89 ± 1.80	15.01 ± 1.76	14.76 ± 1.92	0.482
MCV(fL)	92.12 ± 8.20	90.67 ± 8.14	94.02 ± 8.44	0.063
MCHC(g/dL)	34.93 ± 1.54	34.57 ± 1.55	35.29 ± 1.52	0.098
MCH(pg)	31.05 ± 3.20	30.72 ± 3.13	31.99 ± 3.10	0.533
MPV(fL)	8.46 ± 1.10	8.53 ± 1.11	8.42 ± 1.09	0.864
WBC($x10^9$/L)	7.63 ± 0.71	7.99 ± 0.26	7.52 ± 0.95	0.402
lymphocyte($x10^9$/L)	1.70 ± 0.65	1.62 ± 0.67	1.75 ± 0.65	0.181
Platelet($x10^9$/L)	280 ± 82	289 ± 75	271 ± 86	0.261
PLR > 260(n, %)	39(22.5)	25(32.9)	14(14.4)	**0.004***

The continuous variables are presented as mean (SD),
* : $p < 0.05$.

The final logistic regression model for cancer patients with VTE was presented in Table 2. The result showed an increase of VTE for receiving surgical procedure (OR = 1.537, 95%CI = 1.241-1.984, $p = 0.021$), chemotherapy (OR = 1.969, 95%CI = 1.321-2.225, $p = 0.013$) and the PLR >260 (OR = 2.757, 95%CI = 1.655-3.862, $p = 0.025$). These variables were independent predictors of a VTE episode in patients with cancer. In particular, patients with PLR >260 had an approximately threefold increased risk of developing VTE than PLR ≤ 260.

Discussion

In this study, we retrospectively analyzed the clinical characteristics and laboratory parameters in cancer patients with and without VTE. The results demonstrated that PLR significantly higher in the case of cancer patients with VTE. PLR >260 was strongly associated with the occurrence of VTE, exceeding an approximately threefold increased risk. In addition, surgical procedure and chemotherapy also turned out to be independent risk factor for VTE in cancer patients.

Table 2
The multiple Logistic Regression of cancer patients with VTE.

Variables	B	Wads	OR	95%CI	*p*
Surgery (Yes VS. No)	2.673	1.543	1.537	1.241-1.984	**0.021***
Chemotherapy (Yes VS. No)	1.526	6.571	1.969	1.321-2.225	**0.013***
PLR (>260 VS. ≤260)	2.506	4.965	2.757	1.655-3.862	**0.025***

* : $p < 0.05$