Prognostic Values of Platelet-Associated Indicators in Resectable Lung Cancers

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Abstract

Background: Lung cancer is the leading cause of cancer death. Platelet-related indicators, including platelet count, plateletcrit, mean platelet volume, and platelet distribution width, not only associate with morphology and functions of platelet but also correlate with tumor development and metastasis. In the present study, we investigated the values of platelet-related indicators in the prognosis evaluation of resectable lung cancers. Methods: In total, 101 patients with resectable lung cancer were recruited in this study. Patients were divided into 2 groups according to the median pretreatment values. To evaluate the individual value changes after treatment, we introduced the concept of post-/pretreatment ratio (C2/C1 indicated value was not increased after treatment, while >C1 suggested increased value). Results: The high pretreatment platelet count level was correlated with larger tumor size. High pretreatment plateletcrit level was associated with more lymph nodes metastasis. Patients with high pretreatment plateletcrit level had worse overall survival, whereas pretreatment platelet count, mean platelet volume, and platelet distribution width levels were not correlated with outcomes. Surgery had no impact on the values of platelet count, plateletcrit, mean platelet volume, or platelet distribution width. Adjuvant chemotherapy significantly decreased the values of platelet count and plateletcrit, whereas it had no effect on the values of mean platelet volume or platelet distribution width. Whole course of treatment (surgery combined with adjuvant chemotherapy) significantly decreased the values of platelet count and platelet distribution width, whereas it had no effect on the values of plateletcrit or mean platelet volume. Post-/pretreatment platelet count, plateletcrit, mean platelet volume, and platelet distribution width ratios were not correlated with outcomes. Univariate analyses demonstrated that American Joint Committee on Cancer stage and pretreatment plateletcrit level were significant risk factors for prognosis. Cox regression analysis revealed that no factor independently associated with worse survival. Conclusion: Pretreatment plateletcrit level could be a potential prognostic factor in resectable lung cancers.

Keywords

lung cancer, PLT, PCT, MPV, PDW, prognosis

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**Introduction**

Lung cancer is the second most commonly diagnosed cancer but is the leading cause of cancer-related death. Researchers have indicated that lung cancers take up nearly 27% of total cancer death. There are 2 histological types of lung cancer: small-cell lung cancer (SCLC) and non-small-cell lung cancer (NSCLC). Approximately 80% lung cancers are NSCLC, which includes adenocarcinoma, squamous cell carcinoma and large-cell carcinoma. About 90% occurrence of NSCLC are linked with smoking. Surgical resection is the major choice for patients at early stages.

Platelet-related indicators include platelet count (PLT), plateletcrit (PCT), mean platelet volume (MPV), and platelet distribution width (PDW). In recent years, platelet has been testified to participate in the development and metastasis of cancer. Platelet-related indicators are associated with multiple tumor prognosis, including rectal cancer, pancreatic cancer, gastric cancer, and so on. Previous studies have found that platelet-related indicators in patients with lung cancer are more variable than those in the control group. Maraz and colleagues proved that in patients with resectable lung cancer, there was a negative correlation between high PLTs and overall survival (OS). Zhang and Ran demonstrated that elevated PLT denotes a poor prognosis in patients with lung cancer. Previous studies have indicated that the number and activity of platelets are associated with variety of malignancies. Plateletcrit provides more comprehensive data about total platelet mass because it is the combination of MPV and PLTs, where $PCT = PLT \times MPV/10^7$. Mean platelet volume is a platelet volume index and is recognized as a hallmark of platelet activation. Platelet distribution width is a parameter of variation in platelet size. High PDW level can be a sign of activated platelet production. Elevated platelet release will lead to an increase in the average platelet size and consequently affects the PDW.

In our present study, we aimed to investigate whether platelet-related indicators could provide beneficial prognostic information for patients with resectable lung cancer and whether they have an impact on the patients’ OS.

**Materials and Methods**

**Participants and Inclusion Criteria**

The study was conducted from March 2017 to August 2017 as a retrospective investigation of patients with resectable lung cancer who had been referred to the First Affiliated Hospital of Soochow University (Jiangsu, China) between January 2007 and May 2016. Approval for the study was granted by the Medical Ethics Committees of the First Affiliated Hospital of Soochow University. Clinical and pathological records of all the patients participating in the study were reviewed periodically. The inclusion criteria were as follows: (1) those with histologically or cytologically confirmed resectable lung cancer; (2) age 18 to 70 years; (3) Eastern Cooperative Oncology Group performance status score of ≤1; (4) those with a predicted survival of ≥6 months; (5) those who met the following laboratory criteria: white blood cells (WBCs) ≥4.0 × 10^9/L; absolute neutrophil count ≥ 2.0 × 10^9/L; PLT ≥ 100 × 10^9/L. The inclusion criteria were as follows: the patient failed to complete adjuvant chemotherapy after surgery. Censored data defined as patients whose survival time exceeds the last follow-up time or lost after treatment.

After obtaining informed consent, a total of 101 patients with resectable lung cancer were recruited in the study. All cases were confirmed by surgery and pathology. Patient characteristics are detailed in Table 1. The median age of the 101 patients was 60 years (range, 80-27 years), and 63 patients were males and 38 were females. The pathologic types were divided into NSCLC and SCLC. The staging of cancer was made according to tumor-nodulus-metastases classification and classified through the American Joint Committee on Cancer (AJCC) recommendations. The prognostic analyses were performed regarding OS.

**Blood Samples**

Peripheral venous blood (5-7 mL) was collected into a sterile EDTA tube. All blood samples were fasted and obtained between 6:30 and 7:30 AM in order to standardize the known impact of circulating hormones (circadian rhythm) on the number and subtype distribution of the various WBC indices. Hematological parameters were analyzed within 30 minutes after collection using a hematology analyzer (Sysmex XE-2100; Sysmex, Kobe, Japan). The patients were divided into 2 groups according to the median value of PLT, PCT, MPV, or PDW. The post-/pretreatment ratios were defined as the ratio of pretreatment platelet-related parameter values and the corresponding ones obtained after therapy.

**Evaluation**

Computed tomography scan was performed for the assessment of response every 2 months and evaluated according to the criteria of Response Evaluation Criteria in Solid Tumors 1.1.
| Clinicopathologic Features | PLT       | PCT       | MPV       | PDW       |
|---------------------------|-----------|-----------|-----------|-----------|
| Gender                    | Low, n    | High, n   | χ²        | P Value   |
| Men                       | 63        | 32        | 31        | 0.032     | .858      |
| Women                     | 38        | 20        | 18        | 0.538     | .463      |
| Age, years                | Low, n    | High, n   | χ²        | P Value   |
| ≤56                       | 56        | 27        | 29        | 1.189     | .276      |
| >56                       | 45        | 25        | 20        | 1.815     | .178      |
| Pathologic type           | Low, n    | High, n   | χ²        | P Value   |
| NSCLC                     | 92        | 49        | 43        | 0.256     | .613      |
| SCLC                      | 9         | 3         | 6         | 0.256     | .613      |
| Tumor size, cm            | Low, n    | High, n   | χ²        | P Value   |
| ≤5                        | 73        | 45        | 28        | 10.879    | .001      |
| >5                        | 28        | 7         | 21        | 3.916     | .048      |
| Depth of invasion         | Low, n    | High, n   | χ²        | P Value   |
| T1, T2                    | 77        | 43        | 34        | 3.742     | .053      |
| T3, T4                    | 24        | 9         | 15        | 3.288     | .071      |
| Lymphonodus metastasis    | Low, n    | High, n   | χ²        | P Value   |
| N0, N1                    | 68        | 35        | 33        | 2.416     | .120      |
| N2                        | 33        | 17        | 16        | 3.288     | .071      |
| AJCC stage                | Low, n    | High, n   | χ²        | P Value   |
| I, II                     | 64        | 33        | 31        | 1.228     | .268      |
| III                       | 37        | 19        | 18        | 2.416     | .120      |

Abbreviations: AJCC, American Joint Committee on Cancer; H, high; L, low; MPV, mean platelet volume; NSCLC, non-small-cell lung cancer; PCT, plateletcrit; PDW, platelet distribution width; PLT, platelet count; SCLC, small-cell lung cancer.

*aP < .01.
*bP < .05.
Follow-Up

Survival time generally means OS in oncology, which was measured from the date of diagnosis until death or last clinical evaluation. The prognostic analyses were performed regarding OS. Overall survival was defined as the time from the diagnosed date to death from any cause.

Statistical Analysis

All statistical analyses were performed using SPSS 19.0 software (Chicago, Illinois). For analysis of survival data, Kaplan-Meier curves were constructed, and statistical analysis was carried out using the log-rank test. The associations between blood parameters status and clinicopathologic features were explored by the $\chi^2$ tests. The relationship between changes in the blood parameters status and surgery or chemotherapy were assessed by the $t$ tests. Cox regression analysis was used to identify the independent risk factors associated with resectable lung cancer using a backward elimination technique, which involves including all the independent variables into the equation and gradually eliminating the nonstatistical independent variables to derive a potentially suitable set of predictors. All values of $P < .05$ were considered statistically significant.

Results

Pretreatment PCT Level Predicted Outcomes of Patients With Resectable Lung Cancer

The Kaplan-Meier plots were used to determine the effect of pretreatment PLT, PCT, MPV, and PDW status on OS (Figure 1A-D). The patients were divided into 2 groups according to the median value of PLT (low PLT, $\leq 219.000 \times 10^9/L$ or high PLT $>219.000 \times 10^9/L$), PCT (low PCT $\leq 0.213 \, L/L$ or high PCT $>0.213 \, L/L$), MPV (low MPV $\leq 10.282 \, fl$ or high MPV $>10.282 \, fl$).
or PDW (low PDW ≤ 13.700% or high PDW > 13.700%). The median OS of the high PLT group was 34 (28.121-39.879) months while that of the low PLT group was 34 (28.128-39.872) months (P = .792). The median OS was 32 (25.070-38.930) months in the high-PCT group and 34 (30.002-37.998) months in the low-PCT group (P = .037). The median OS of the high MPV group was 34 (30.535-37.465) months while that of the low MPV group was 32 (24.237-39.763) months (P = .782). The median OS of the high-PDW group was 34 (30.535-37.465) months while that of the low MPV group was 32 (24.237-39.763) months (P = .782). The median OS was 35 (26.915-43.085) months in the high-PDW group and 30 (24.237-39.763) months in the low-PDW group (P = .173). Thus, the patients whose PCT levels were higher before treatment had worse prognosis. However, pretreatment levels of PLT, MPV, or PDW had no effects on OS.

**Effects of Surgery on the Values of Platelet-Related Indicators**

The effects of surgery on the levels of platelet-related indicators were presented in Figure 2A-D, respectively. The median value of PLT was 219.000 × 10^9/L (213.257 × 10^9/L-224.743 × 10^9/L) before surgery and 211.000 × 10^9/L (198.690 × 10^9/L-223.310 × 10^9/L) after surgery (P = .540). The median value of PCT was 0.210 L/L (0.200-0.230 L/L) before surgery and 0.210 L/L (0.200-0.230 L/L) after surgery (P = .440). The median value of MPV was 10.270 fl (9.740-10.700 fl) before surgery and 10.200 fl (9.700-10.600 fl) after surgery (P = .330). The median value of PDW was 13.700% (13.080%-15.600%) before surgery and 14.000% (12.800%-15.450%) after surgery (P = .215). Therefore, surgery had no significant impact on the values of PLT, PCT, MPV, and PDW.

**Effects of Adjuvant Chemotherapy on the Values of Platelet-Related Indicators**

The effects of adjuvant chemotherapy on the status of platelet-related indicators were shown in Figure 3A-D. The median value of PLT was 211.000 × 10^9/L (198.690-223.310 × 10^9/L) before adjuvant chemotherapy and 184.000 × 10^9/L (176.840-191.160 × 10^9/L) after adjuvant chemotherapy (P = .000). The median value of PCT was 0.210 L/L (0.200-0.230 L/L) before adjuvant chemotherapy and 0.190 L/L (0.180-0.200 L/L) after adjuvant chemotherapy (P = .003). The median value of MPV was 10.200 fl (9.700-10.600 fl) before adjuvant chemotherapy and 10.200 fl (9.700-10.500 fl) after adjuvant chemotherapy (P = .570). The median value of PDW was 14.000% (12.800%-15.450%) before adjuvant chemotherapy and 12.510% (11.950%-14.450%) after adjuvant chemotherapy (P = .053). Therefore, adjuvant chemotherapy significantly decreased the values of PLT and PCT, whereas it had no significant impact on the values of MPV or PDW.
Effects of Whole Course of Treatment on the Values of Platelet-Related Indicators

The impact of whole course of treatment (surgery and adjuvant chemotherapy) on the values of the platelet-related indicators were presented in Figure 4 A-D. The median value of PLT was 219,000 $\times 10^9$/L (213,257-224,743 $\times 10^9$/L) before treatment and 184,000 $\times 10^9$/L (176,840-191,160 $\times 10^9$/L) after treatment ($P = .005$). The median value of PCT was 0.210 L/L (0.190-0.230 L/L) before treatment and 0.190 L/L (0.180-0.200 L/L) after treatment ($P = .055$). The median value of MPV was 10.270 fl (9.740-10.700 fl) before treatment and 10.200 fl (9.700-10.500 fl) after treatment ($P = .337$). The median value of PDW was 13.700% (13.080%-15.600%) before treatment and 12.510% (11.950%-14.450%) after treatment ($P = .011$). Thus, whole course of treatment significantly decreased the values of PLT and PDW, whereas it had no obvious effect on the value of PCT or MPV.

Changes in PLT, PCT, MPV, and PDW Levels After Whole Course of Treatment Were not Correlated with the Outcomes of Patients With Resectable Lung Cancer

The Kaplan-Meier plots were used to determine the effect of changes of the PLT, PCT, MPV, and PDW status on OS (Figure 5A-D). The median OS of patients whose PLT level increased following whole course of treatment was 27 (22.981-31.019) months while that of the not-increased PLT group was 37 (31.951-42.049) months ($P = .228$). The median OS of patients whose PCT level increased following whole course of treatment was 29 (24.641-33.359) months while that of the not-increased PCT group was 36 (32.578-39.422) months ($P = .808$). The median OS of patients whose MPV level increased following whole course of treatment was 33 (26.575-39.425) months while that of the not-increased MPV group was 34 (29.738-38.262) months ($P = .876$). The median OS of patients whose PDW level increased following whole course of treatment was 32 (25.143-38.857) months while that of the not-increased PDW group was 34 (30.566-37.434) months ($P = .567$). Thus, changes in PLT, PCT, MPV, and PDW levels upon treatment had no significant effects on OS.

Prognostic Factors for Resectable Lung Cancer

Univariate analyses demonstrated that AJCC stage III (hazard ratio [HR]: 1.538; 95% confidence interval [CI]: 1.010-2.340; $P = .045$) and high pretreatment PCT level (HR: 1.522; 95% CI: 1.013-2.287; $P = .043$) were significant risk factors for a poor prognosis (Table 2). However, gender, age, pathologic type, tumor size, depth of invasion, lymphonodus metastasis, and post-/pretreatment other platelet-related indicators had no significance to the prognosis (Table 2). In Cox regression analysis, we found no factor was independently associated with worse survival.
Platelets play an integral role in the development and metastasis of cancer.\textsuperscript{6,20} Platelet parameters, including PCT, MPV, and PDW, closely relate to the function and activation of platelets.\textsuperscript{7,14,21,22} Previous studies have confirmed that platelet-related indicators were associated with prognosis of tumors.\textsuperscript{7,12,23} Maraz and colleagues proved that there was a negative correlation between high PLTs (≥400.00 × 10\textsuperscript{9}/L) and OS in patients with resectable lung cancer.\textsuperscript{24} Once activated, platelets can bind to tumor cells via P-selectin which presents on the surface of platelets and bind to CD24 ligand.\textsuperscript{25,26} In addition, platelets facilitate tumor growth and metastasis through releasing proangiogenic and growth factors.\textsuperscript{25} For instance, activated platelets promote metastasis by secreting lysosphatidic acid (LPA), a lipid that has growth factor–like properties and plays a role in many cellular processes including cell proliferation, survival, migration, tumor cell invasion, and reversal of differentiation.\textsuperscript{27} Furthermore, platelet is a primary source of vascular endothelial growth factor, a growth factor that increases vascular permeability, promotes extravasation, and is critical for angiogenesis.\textsuperscript{28} Finally, tumor-derived platelets also predispose patients with cancer to thrombotic events. Venous thromboembolism and high PLTs are risk factors associated with poor prognosis in patients with cancer.\textsuperscript{9,29-31} In our present study, both surgery and adjuvant chemotherapy significantly reduced the level of PLT, although pretreatment level and post-/pretherapeutic ratio of PLT had no significant effects on OS.

Plateletcrit, which is the combination of 2 aspects including PLT and MPV, is the percentage of blood volume covered by platelets and is a relevant parameter to assess platelet status.\textsuperscript{14,22} Ozaksit et al proved that the value of PCT is higher in patients with epithelial ovarian cancer compared to the healthy controls.\textsuperscript{32,33} Besides, high PCT was associated with worse prognosis in patients with pancreatic adenocarcinoma who received intensity-modulated radiation therapy.\textsuperscript{34} Interestingly, negative correlations were observed between the induced frequency of micronuclei and PCT in differentiated patients with thyroid cancer undergoing radioactive iodine (\textsuperscript{131}I) treatment following thyroid and lymph node surgery. Therefore, PCT may be used as a biomarker for diagnosis, prognosis, and radiosensitivity in certain cancers.\textsuperscript{35} Oncel et al certified that the PCT values of patients with metastatic lung cancer were higher than those of patients without metastasis. While comparing to healthy controls, the value of PCT was lower.\textsuperscript{36} In the present study, we found that the contribution of the downregulation of PCT could be mainly made by chemotherapy since surgery had no effect on PCT status. Moreover, patients with low pretreatment level of PCT had better outcomes. Univariate analyses demonstrated that high pretreatment PCT level was a significant risk factors for a poor prognosis. Although basing on changes in individual PCT levels, post-/pretherapeutic ratio

**Discussion**

Platelets play an integral role in the development and metastasis of cancer.\textsuperscript{6,20} Platelet parameters, including PCT, MPV and PDW, closely relate to the function and activation of platelets.\textsuperscript{7,14,21,22} Previous studies have confirmed that platelet-related indicators were associated with prognosis of tumors.\textsuperscript{7,12,23} Maraz and colleagues proved that there was a negative correlation between high PLTs (≥400.00 × 10\textsuperscript{9}/L) and OS in patients with resectable lung cancer.\textsuperscript{24} Once activated, platelets can bind to tumor cells via P-selectin which presents on the surface of platelets and bind to CD24 ligand.\textsuperscript{25,26} In addition, platelets facilitate tumor growth and metastasis through releasing proangiogenic and growth factors.\textsuperscript{25} For instance, activated platelets promote metastasis by secreting lysosphatidic acid (LPA), a lipid that has growth factor–like properties and plays a role in many cellular processes including cell proliferation, survival, migration, tumor cell invasion, and reversal of differentiation.\textsuperscript{27} Furthermore, platelet is a primary source of vascular endothelial growth factor, a growth factor that increases vascular permeability, promotes extravasation, and is critical for angiogenesis.\textsuperscript{28} Finally, tumor-derived platelets also predispose patients with cancer to thrombotic events. Venous thromboembolism and high PLTs are risk factors associated with poor prognosis in patients with cancer.\textsuperscript{9,29-31} In our present study, both surgery and adjuvant chemotherapy significantly reduced the level of PLT, although pretreatment level and post-/pretherapeutic ratio of PLT had no significant effects on OS.

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**Figure 4.** Relationship between changes in status of pretreatment platelet-related indicators and whole course of treatment. A, Whole course of treatment decreased the value of PLT. B, Whole course of treatment had no obviously influence on the value of PCT. C, Whole course of treatment had no obviously influence on the value of MPV. D, Whole course of treatment decreased the value of PDW. *P < .05; **P < .01. MPV indicates mean platelet volume; PCT, plateletcrit; PDW, platelet distribution width; PLT, platelet count.
of PCT had no significant effects on OS, low PCT level before treatment could be a favorable prognostic index.

Mean platelet volume, a common parameter of platelet size, could be used as an index of activated platelet. Multiple investigators have reported that increased MPV could be detected in acute myocardial infarction, unstable angina, and stroke. In addition, this index is also investigated in a variety of malignant tumors. According to the report from Baldane et al, the level of MPV in patients with thyroid cancer was significantly higher when compared to benign goiters or healthy controls. Similar results have also been found in colorectal cancers. Nevertheless, a research reported that MPV was higher in lung cancers at early stages (stage I-II) than healthy controls. Previous studies have also pointed out that high MPV level is closely related to inflammatory response. As an inflammation marker, high MPV level is correlated with various malignant tumors, such as endometrial cancer, gastric cancer, and thyroid cancer. Previous researches have demonstrated that several inflammatory factors, such as interleukin (IL) 1, IL-3 and IL-6 can promote the proliferation of macrophages and further lead to increased platelet level. Many tumor tissues can detect the elevated levels of IL-6, including lung cancer. Thus, cancer-induced changes in MPV status could be due to response to inflammatory stimuli. However, in our present study, we found that neither surgery nor adjuvant chemotherapy could affect MPV level. Besides, pretreatment level and post-/pretherapeutic ratio of MPV had no significant effects on OS.

Previous investigations concerning PDW are controversial. In a study of Emel Kurtoglu, the PDW level significantly decreased in the patients with endometrial cancer compared to the healthy group. However, Gunaldi and colleagues demonstrated that high PDW level is positively correlated with metastasis of gastric cancer. Hirahara et al proved that PDW levels and prognosis of esophageal cancer had no statistically significant relationship. In the present study, although treatment significantly decreased the value of PDW, pretreatment level, and post-/pretherapeutic ratio of PDW had no significant impact on OS.
Table 2. Univariate and Multivariate Logistic Regression Analysis of Resectable Lung Cancer Risk Factors.

| Risk Factors                                      | Overall Survival (OS) | Univariate Analysis | Multivariate Analysis |
|--------------------------------------------------|-----------------------|---------------------|----------------------|
|                                                  | OR (95% CI)           | P Value             | OR (95% CI)           | P Value             |
| Gender (women or men)                            | 0.782 (0.517-1.183)   | .245                | –                    | –                   |
| Age (>60 years or ≤60 years)                     | 1.059 (0.713-1.572)   | .776                | –                    | –                   |
| Pathologic type (NSCLC or SCLC)                  | 0.890 (0.446-1.774)   | .740                | –                    | –                   |
| Tumor size, cm (>5 or ≤5)                        | 0.851 (0.546-1.326)   | .476                | –                    | –                   |
| Depth of invasion (T3-4 or T1-2)                 | 1.126 (0.708-1.789)   | .617                | –                    | –                   |
| Lymphonodus metastasis (N2 or N0 – 1)            | 1.474 (0.959-2.264)   | .077                | –                    | –                   |
| AJCC stage (III or I-II)                         | 1.538 (1.010-2.340)   | .045<sup>a</sup>    | 1.453 (0.963-2.191)   | .075                |
| Pretreatment PLT (>219,000 x 10<sup>9</sup>/L or ≤219,000 x 10<sup>9</sup>/L) | 0.949 (0.638-1.411)   | .796                | –                    | –                   |
| Pretreatment PCT (>0.213 L/L or ≤0.213 L/L)      | 1.522 (1.013-2.287)   | .043<sup>a</sup>    | 1.460 (0.956-2.229)   | .080                |
| Pretreatment MPV (>10.282 fl or ≤10.282 fl)     | 0.947 (0.637-1.406)   | .787                | –                    | –                   |
| Pretreatment PDW (>13.700% or ≤13.700%)         | 0.764 (0.513-1.136)   | .184                | –                    | –                   |
| Post-pretreatment PLT ratio (>1 or ≤1)           | 1.290 (0.844-1.972)   | .239                | –                    | –                   |
| Post-pretreatment PCT ratio (>1 or ≤1)           | 0.951 (0.630-1.436)   | .812                | –                    | –                   |
| Post-pretreatment MPV ratio (>1 or ≤1)           | 0.969 (0.650-1.445)   | .879                | –                    | –                   |
| Post-pretreatment PDW ratio (>1 or ≤1)           | 0.888 (0.585-1.347)   | .576                | –                    | –                   |

Abbreviations: AJCC, American Joint Committee on Cancer; CI, confidence interval; MPV, mean platelet volume; NSCLC, non-small-cell lung cancer; OR, odds ratio; PCT, plateletcrit; PDW, platelet distribution width; PLT, platelet count; SCLC, small-cell lung cancer.

<sup>a</sup>P < .05.

In conclusion, our data showed that low PCT level before treatment had better OS in patients with resectable lung cancer. This noninvasive, simple, and low-cost biomarker may be a prognostic indicator. The limitations of our study may include its retrospective design, data coming from single center, and insufficiency of case number.

Authors’ Note

Jing-Jing Wang, Yin-Ling Wang, and Xin-Xin Ge contributed equally to this work. After obtaining informed consent, a total of 101 resectable patients with lung cancer were recruited in the study. The study was conducted from March 2017 to August 2017 as a retrospective investigation of resectable lung cancer patients that had been referred to the First Affiliated Hospital of Soochow University (Jiangsu, China) between Jan 2007 and May 2016. Our study was approved by the Medical Ethics Committees of the First Affiliated Hospital of Soochow University (approval Batch No. 236). All patients provided written informed consent prior to enrollment in the study.

Declaration of Conflicting Interests

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