The role of lymphocyte count in the early diagnosis of surgical site infection following posterior lumbar fusion

L.-S. JI[1], T.-S. LU[1], Y.-P. WANG[2], Y.-J. JIA[1], J.-W. YANG[1], Y. MA[3], H.-E. LIU[4], C.-S. LUO[1]

[1]Department of Spine Surgery, Guizhou Province Orthopedic Hospital, Guiyang, Guizhou, China
[2]Department of Gastroenterology, Guizhou Province Orthopedic Hospital, Guiyang, China
[3]Department of Orthopedics, Nanyang Central Hospital, Nanyang, Henan, China
[4]Department of Infectious Disease, Kunming Medical University First Affiliated Hospital, Kunming, Yunnan, China

L.-S. Ji and T.-S. Lu are equal contributors

Abstract. – OBJECTIVE: This study aimed to explore the early diagnostic value of lymphocyte count in the early diagnosis of surgical site infection (SSI) following posterior lumbar fusion.

PATIENTS AND METHODS: In this study, we retrospectively analyzed the data from a total of 37 patients with lumbar SSI from Guizhou Province Orthopaedic Hospital and Nanyang Central Hospital, 2008.1-2018.11, and 104 patients without SSI. We analyzed the C-reactive protein (CRP) level, white blood cell count (WBC) and differential count before instrumented lumbar fusion at 3 and 7 days postoperatively. The significance of the differences was evaluated by one-way ANOVA, followed by Fisher's test. The parameters mentioned above were analyzed on postoperative days 3 and 7 using the receiver operating characteristic curve and the area under the curve (AUC). Furthermore, the analyses were conducted by SPSS 22.0 software.

RESULTS: The lymphocyte count in the SSI group on postoperative day 3 was significantly lower than that in the no-SSI group after surgery (*p*=0.000). According to the ROC curve analysis of related parameters on postoperative day 3, the AUC value of lymphocytes (0.840) was significantly larger than the AUC value of C-reactive protein (0.749).

CONCLUSIONS: The lymphocyte count and C-reactive protein level on postoperative day 3 are reliable predictors of infection.

Key Words:
Lymphocyte count, Neutrophil count, C-reactive protein, Surgical site infection.

Abbreviations

SSI: surgical site infection; CRP: C-reactive protein; WBC: white blood cell count; AUC: the area under the curve.

Introduction

One of the most common complications following spinal fusion is surgical site infections (SSIs). Infection rates following spinal instrumentation surgery are reported to be around 0.7% to 12%[1]. These infections are typically treated with surgical debridement or revision[2]. Invasion or even revision can induce higher postoperative complications, prolong hospitalization, and affect the prognosis and postoperative rehabilitation[3]. Therefore, the early diagnosis and prevention of infection in spinal surgery patients are of great value for postoperative rehabilitation[4]. Previous scholars[5] have confirmed that surgical factors are not affected and are reliable predictors of infection after spinal fusion. The purpose of this study was to investigate the utility of lymphocyte count in the early diagnosis of infection following lumbar fusion by analyzing the changes in lymphocyte count at 3 and 7 days postoperatively in patients who underwent lumbar fusion.

Patients and Methods

Patients

This research project obtained conformation from the institutional review boards of Guizhou Province Orthopedic Hospital, approval No. LW20181015. 37 patients with SSI who had spinal fusion surgery at the Hospital's Department of Spinal Surgery between January 2008 and November 2018 were analyzed retrospectively; 104 patients without postoperative infection at the surgical site were included as control subjects. The exclusion criteria were as follows: (1) patients with an infection before

Corresponding Authors: Huai-e Liu, MD; e-mail: liuhuaie@163.com
Chunshan Luo, MD; e-mail: chunyi58870403@163.com

surgery; (2) patients who experienced preoperative trauma; (3) patients with preoperative malignant tumors, diabetes, rheumatoid arthritis, or other immune diseases; (4) patients who took antibiotics within one week of surgery; (5) patients 18 or more years old; (6) patients who did not have regular blood and C-reactive protein tests; (7) patients with exudate involving cerebrospinal fluid, liquified fat or other fluids. All patients received routine preventive prescriptions for cefuroxime sodium or cefazolin sodium antibiotics 30 minutes before surgery. If the operation time exceeded three hours, we used an additional antibiotic and the same antibiotic to prevent infection within two days after surgery.

The C-reactive protein (CRP) level, white blood cell (WBC) count, neutrophil and lymphocyte counts, and neutrophil and lymphocyte percentages were recorded prior to surgery and 1, 3, and 7 days postoperatively. Additionally, the duration of the operation, intraoperative blood loss, and number of fusion segments were recorded.

Statistical Analysis

SPSS 22.0 (IBM Corp., Armonk, NY, USA) was used to analyze differences in CRP, WBC, neutrophil counts, and lymphocyte counts. One-way ANOVA was used to evaluate the significance of the differences. We plotted the ROC curves of various parameters, such as the lymphocyte count, CRP level and WBC count, recorded at 3 and 7 days postoperatively and calculated the area under the curve. The enumerated data and measurement data were examined by χ^2-test and *t*-test and expressed as [n (%)] and ($\bar{x}\pm s$). $p<0.05$ was assumed as a statistical difference.

Results

This study included 104 patients without lumbar spine SSI and 37 patients with SSI after lumbar fusion surgery. In the SSI and non-SSI groups, the median age at surgery was (64.84±7.281) and (63.22±9.608) years, respectively. The average operating times for the SSI group and the non-SSI groups were (164.626±50.32) minutes and (165.661±47.917) minutes, respectively, and the average amount of blood lost was (436.238±115.981) and (431.616±150.022), respectively. The number of fused segments in the SSI and non-SSI groups was (1.59±0.643) and (1.51±0.732), respectively. There were no significant differences between the two groups in regard to age, gender, operating time, intraoperative blood loss, or the number of fused segments (Table I).

No significant differences were observed in the WBC count (p=0.418), neutrophil count (p=0.368), or lymphocyte count (p=0.213) before the operation. The WBC count (p=0.003), CRP level (p=0.000), neutrophil percentage (p=0.018) and neutrophil count (p=0.000) significantly differed between the two groups at three days postoperatively. However, the lymphocyte count (p=0.000) was significantly lower in the infected patients at three days postoperatively (Table II). According to the ROC curve analysis of related parameters at three days postoperatively, only the lymphocyte count and CRP level have diagnostic value for patients with infection after surgery. The total area under the curve (AUC) value for lymphocytes (0.840) was significantly larger than that for CRP (0.749) (Table III , Figures 1-2). The Youden index of lymphocyte count (0.644; critical value 1.16×10^9/L) was significantly higher than that of the CRP level (0.398; critical value 26.2 mg/L). Therefore, at three days after lumbar surgery, when the CRP level >26.2 mg/L and the lymphocyte count $<1.16\times10^9$/L, it is highly suspected that there is an infection in patients (Table IV and Figure 2).

Discussion

After spinal fusion, infection is likely to cause severe consequences, leading to low clinical

Table I. Patient data ($\bar{x}\pm s$).

	SSI group (N=37)	Non-SSI group (N=104)	*p*
Age (years)	64.84±7.281	63.22±9.608	0.201
Sex (Male/Female)	19/18	51/53	0.810
Operating time (min)	164.626±50.320	165.661±47.917	0.768
Blood loss volume (mL)	436.238±115.981	431.616±150.022	0.636
Number of fused segments	1.59±0.643	1.51±0.732	0.170

SSI, surgical site infection.

Table II. Results of statistical analysis between the SSI and no-SSI Groups ($\bar{x}\pm s$).

	Non-SSI group (N=104)	SSI group (N=37)	p
White blood cell count			
Before Surgery	6.191±1.638	6.408±1.348	0.418
POD1	9.843±2.895	11.822 ±4.330	0.005
POD3	8.976±2.478	10.669±3.589	0.003
POD7	7.142±2.012	9.184±3.572	0.001
Neutrophil percentage (%)			
Before Surgery	59.174±8.018	61.818±4.416	0.121
POD1	74.047±7.753	81.124±8.969	0.000
POD3	75.620±6.409	78.931±6.604	0.018
POD7	66.079±8.524	76.924±8.494	0.000
Neutrophil count			
Before Surgery	4.539±1.142	4.759±0.750	0.368
POD1	7.095±2.039	9.037±3.890	0.007
POD3	6.649±2.079	9.451±3.905	0.000
POD7	4.909±1.490	6.615±2.908	0.000
Lymphocyte percentage			
Before Surgery	36.072±8.171	33.726±7.139	0.089
POD1	14.137±4.433	11.113±5.093	0.001
POD3	15.493±5.133	10.399±3.553	0.000
POD7	18.795±5.271	20.184±6.551	0.297
Lymphocyte count			
Before Surgery	2.126±0.584	1.973±0.380	0.213
POD1	1.585±0.508	1.293±0.533	0.004
POD3	1.311±0.425	0.848±0.181	0.000
POD7	1.552±0.571	1.165±0.369	0.000
C-reactive protein level			
Before Surgery	1.716±1.362	1.940±1.400	0.357
POD1	39.708±22.570	52.644±33.420	0.060
POD3	38.145±18.590	67.815±35.046	0.000
POD7	21.678±12.833	40.196±25.226	0.000

SSI indicates surgical site infection, and POD indicates postoperative day.

Table III. Results of the test for non-correlation (using Pearson Correlation Coefficient) in the No-SSI Group.

	Operating Time	Intraoperative Blood Loss	Number of Fusion Segments	Noncorrelation for All Factors
CRP at 1 day postoperatively	0.666	0.513	0.265	Yes
Neutrophil percentage at 3 days postoperatively	0.998	0.796	0.400	Yes
Lymphocyte percentage at 3 days postoperatively	0.947	0.070	0.714	Yes
Lymphocyte count at 3 days postoperatively	0.673	0.208	0.040	No
CRP at 3 days postoperatively	0.388	0.064	0.960	Yes
Neutrophil percentage at 7 days postoperatively	0.931	0.802	0.414	Yes
Lymphocyte percentage at 7 days postoperatively	0.565	0.341	0.212	Yes
Lymphocyte count at 7 days postoperatively	0.906	0.390	0.685	Yes
CRP at 7 days postoperatively	0.752	0.987	0.919	Yes

SSI, surgical site infection.

efficacy, physiological and psychological burdens for patients, and economic losses for patients, and the internal fixation device is even removed in some cases[6,7]. Therefore, the early diagnosis of infection is very important[4,8]. If the condition is diagnosed early, antibiotics and other treatments can be used to prevent the need for implant removal[9]. Infection can be diagnosed early on the basis of the type of fever, test results, and local symptoms of the incision (tenderness, redness, purulence, etc.)[10]. However, in recent years, the incision has often been covered with surgical dressings, which leads to a longer observation time of the surgical incision and an increased risk of a delayed diagnosis of infection[11,12]. Kimura et al[13] observed that patients are potentially in an

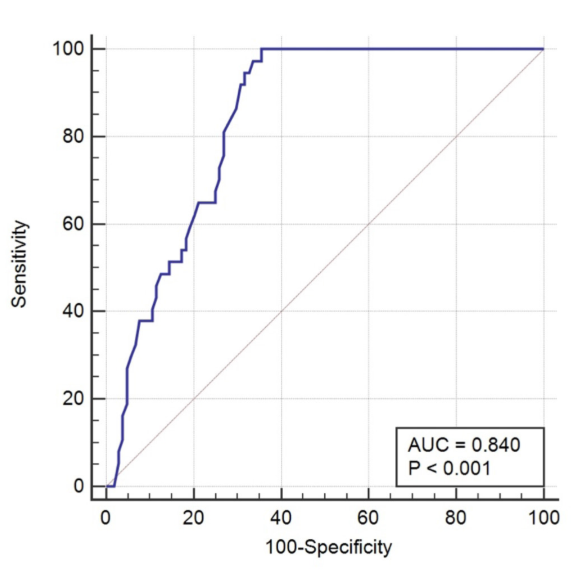

Figure 1. ROC curve used to calculate diagnostic cutoff for lymphocyte count at 3 days postoperatively (p<0.001). Cut-off=1160/µL; sensitivity=64.4%; specificity=100%; AUC=0.840.

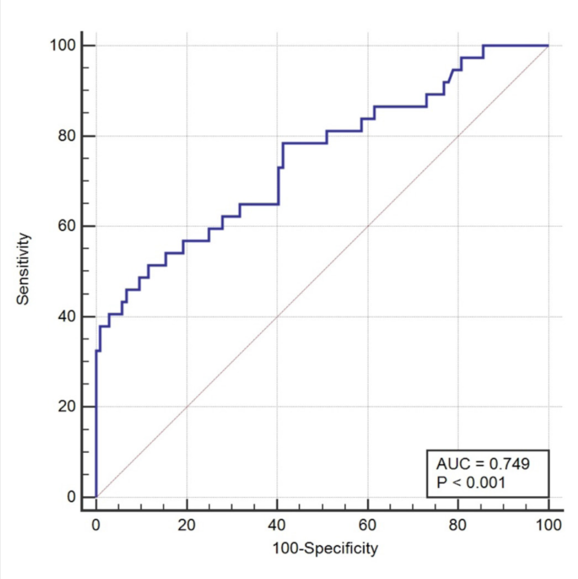

Figure 2. ROC curve used to calculate diagnostic cutoff for C-reactive protein level at 3 days postoperatively (p<0.001). Cutoff=26.2 mg/L; sensitivity=51.35%; specificity=88.46%; AUC=0.749.

Table IV. Sensitivity and specificity of each laboratory marker.

	Sensitivity	Specificity	*p*
(1) Greater elevation of white blood cell count at 7 than at 3 days postoperatively	74%	19.9%	0.391
(2) Greater elevation of CRP level at 7 than at 3 days postoperatively	80.8%	13.5%	0.931
(3) CRP level of >26.2 mg/dL at 3 days postoperatively	51.35%	88.46%	0.001
(4) Neutrophil count of >7.97 at 3 days postoperatively	74.0%	67.6%	0.000
(5) Lymphocyte count of <1,160/µL at 3 days postoperatively	56.7%	91.9%	0.000

SSI, surgical site infection.

immunosuppressive state after surgery. However, the incision does not show obvious local symptoms. The body's resistance to bacteria may have decreased significantly; moreover, these patients may be more susceptible to postoperative infection than those with normal total lymphocyte values.

The CRP level, WBC count and WBC classification are the most commonly used reference indicators of inflammation. Lymphocytes are mainly produced by lymphocytes composed of B cells and T cells (CD4/CD8). The lymphocyte count in peripheral blood is reduced due to the apoptosis of lymphocytes after the operation. Lymphopenia, especially involving helper T cells, may decrease immunity, increasing the chance of infection[14]. Warny et al[15] confirmed that lymphopenia was linked to an increased risk of infection-related hospitalization and infection-related mortality in the general population. A study of 753 intensive care unit (ICU) patients showed that the decrease in lymphocytes at admission and their continuing decline on the third day was related to an increased risk of ICU-acquired infections. The continued decrease in lymphocytes predicted an increased risk of death within 28 days. The lymphocyte count upon ICU admission and on the third day of admission can be used as predictors of immunosuppression[16]. Iwata et al[5] confirmed that the lymphocyte count on the fourth day and the seventh day after surgery and the CRP level on the seventh day postoperatively were predictive markers for predicting infection after spinal fusion. Kuroiwa et al[17] discovered that the CRP value, total white blood cell count, and differential count are reliable signals for the early diagnosis of SSI after spinal instrumented fusion because they are unaffected by operating factors. The lymphocyte count is available on the fourth day after surgery for early infection screening due to its great sensitivity and simplicity of detection[5]. According to research by Takahashi et al[18] and Iwata et al[19], a lymphocyte percentage or lymphocyte count < 1,000/L on the fourth day following surgery may indicate immunosuppression and an increased risk of infection, as these parameters predict high susceptibility to postoperative infection. We found the area under the ROC curve of the lymphocyte count on the third postoperative days to be 0.840 and 0.717, respectively, indicating that the sensitivity of the lymphocyte count was higher on the third day after surgery, so the lymphocyte count on the third day after surgery can be regarded as a more sensitive indicator of the early stage of infection.

Interleukin-6 mediates CRP in hepatocyte synthesis. In addition to infection, surgical injury can increase the CRP level[20,21]. The CRP level peaked on the third day after surgery and rapidly decreased to an average level on the 10th day after surgery. We analyzed the CRP level on the third day and the seventh day after surgery. The areas under the ROC curve were 0.749 and 0.726 on the third and seventh days, respectively, and both values showed high sensitivity. The C-reactive protein level on the third and seventh days can be used as an early indicator of infection. In a study by Iwata et al[19], the area under the CRP ROC curve at seven days after surgery was 0.95, which indicates high sensitivity, although the sample size differed between that study and our study[5].

Historically, inflammatory markers were frequently shown to be influenced by surgical parameters such as surgical duration and blood loss[22,23]. Current research has confirmed that some indicators are unaffected by surgical parameters and have a high value for early diagnosis[5,18]. In this study, we found that the lymphocyte count on the third day after surgery and the CRP level on the third and seventh days after surgery are the most reliable infection-sensitive indicators after lumbar fusion. These indicators are not influenced by operational factors.

Conclusions

In order to evaluate the level of predictive power possessed by each measure, we computed the sensitivity and specificity of a number of different laboratory markers. The lymphocyte count in the SSI group on postoperative day 3 was considerably lower than that in the no-SSI group after surgery. “The lymphocyte count <1.16×10^9/L at 3 days postoperatively” have diagnostic value for patients with infection after surgery.

Informed Consent

All subjects included in the study had signed informed consent.

Ethics Approval

This study was approved by the Ethics Committee of Guizhou Province Orthopedic Hospital, approval No. LW20181015.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Authors’ Contributions

L.-S. Ji, J.-W. Yang and H.-E Liu designed the study and developed the research questions. T.-S. Lu, Y.-P. Wang, Y.-J. Jia and Y. Ma performed the experiments and collected the data. L.-S. Ji, T.-S. Lu, Y.-P. Wang and C.-S. Luo analyzed the data and conducted statistical analyses. L.-S. Ji, T.-S. Lu, C.-S. Luo and H.-E Liu wrote the paper and prepared the figures and tables.

Conflict of Interest

The authors declare that they have no conflict of interest.

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