International Immunopharmacology 74 (2019) 105705

Contents lists available at ScienceDirect

International Immunopharmacology

journal homepage: www.elsevier.com/locate/intimp

Predictive value of post-operative neutrophil/lymphocyte count ratio for surgical site infection in patients following posterior lumbar spinal surgery

Chao-Jun Shen[a], Tao Miao[a], Zhang-Fu Wang[a], Zhen-Fa Li[b], Ling-Qin Huang[a], Ting-Ting Chen[a], Wei-Hua Yan[b,*]

[a] Department of Spine Surgery, TaiZhou Hospital of Zhejiang Province, Wenzhou Medical University, Linhai, Zhejiang 317000, China
[b] Medical Research Center, TaiZhou Hospital of Zhejiang Province, Wenzhou Medical University, Linhai, Zhejiang 317000, China

ARTICLE INFO

Keywords:
White blood cell
White blood cell subsets
C-reactive protein
Surgical site infection
Lumbar
Surgery

ABSTRACT

Objective: Surgical site infection (SSI) is a common complication in patients following posterior lumbar spinal surgery. Various laboratory data such as laboratory parameters derived neutrophil/lymphocyte count ratio (NLR), have been applied for the prediction of SSI, but more studies are necessary to evaluate the significance of these indicators. Here, our study aims to investigate the predictive value of total white blood cells (WBCs), count and percentages of neutrophils and leukocytes, NLR, and C-reactive protein (CRP) for surgical site infection (SSI) in patients after posterior lumbar spinal surgery.

Methods: A total of 293 patients who underwent posterior lumbar spinal surgery were enrolled in this study. Each patient's medical history was retrospectively reviewed, and patients were divided into the deep SSI group (n = 13) and the non-SSI group (n = 280). Laboratory data including total WBC, count and percentages of neutrophils and leukocytes, NLR at 1 week before the operation and the 4 and 7 days post-operation, and CRP at 4 and 7 days post-operation were analysed between the SSI and non-SSI groups. Moreover, predictive power and cut-off of NLR for SSI were determined by receiver operating characteristic curve (ROC) results.

Results: Data revealed that the medians of NLR were markedly increased in the SSI group as compared to that in non-SSI group at 4 days ($p = 0.011$) and 7 days ($p = 0.047$) post-operation. Moreover, the neutrophil percentage was also dramatically increased in the SSI group at both 4 and 7 days post-operation ($p = 0.010$ and $p = 0.030$) respectively compared to the non-SSI group. However, no significant difference was observed between the groups 1 week before the operation. ROC results showed that NLR at 4 days (cut-off > 5.19; sensitivity: 61.5%; specificity: 77.6%; AUC = 0.708) and 7 days (cut-off > 3.85; sensitivity: 69.2%; specificity: 62.7%; AUC = 0.663) post-operation could significantly discriminate the SSI and non-SSI groups. Logistic regression analysis showed that NLR at both post-operative time points (OR = 1.218; $p = 0.003$ and OR = 1.296; $p = 0.048$) could be valuable predictors for SSI.

Conclusion: NLR at 4 and 7 days post-operation are valuable laboratory predictors for SSI in patients with posterior lumbar spinal surgery.

1. Introduction

Posterior lumbar spinal surgery is a routine and effective operation for degenerative diseases; however, complications occur in some patients after the operation [1]. Surgical site infection (SSI) is one of the serious complications after posterior lumbar surgery. SSI generally results in poor clinical outcomes, additional expenses, and even damages to the patient's satisfaction with the medical experience [2,3].

Various measures have been applied for SSI prophylaxis, such as continuously improving on general surgery protocols, anaesthesiology standards and reducing risk factors associated with SSI [4]. Despite these efforts to prevent SSI, the incidence of SSI remains high and ranges from 0.7% to 11.9%, depending on the type of operation and complexity of the procedure reported in previous studies [5]. Thus, besides an initial diagnosis by a surgeon or assessment with imaging equipments, which can effectively determine whether SSI occurs or not. Other indicators, such as the relevant clinical laboratory markers are also of great value in prediction and monitoring of SSI [6,7].

In this scenario, post-operative clinical laboratory markers, such as acute phase-related C-reactive protein (CRP), have been widely used as

* Corresponding author at: Medical Research Center, TaiZhou Hospital of Zhejiang Province, Linhai, Zhejiang 317000, China.
E-mail address: yanwhcom@yahoo.com (W.-H. Yan).

https://doi.org/10.1016/j.intimp.2019.105705
Received 26 March 2019; Received in revised form 13 June 2019; Accepted 14 June 2019
Available online 19 June 2019

inflammatory markers. Additionally, the predictive value for the diagnosis of early SSI with the count and percentage change of peripheral white blood cells (WBCs) and their subsets at different time points after spinal surgery have been emphasized [8]. Iwata et al. [8] indicated that lymphocyte counts on the 4th and 7th days after surgery and CRP levels on the 7th day after surgery were the most reliable laboratory markers for SSI after posterior lumbar surgery. Another marker, the neutrophil/lymphocyte count ratio (NLR), is of clinical significance as an infection or inflammation indicator [9]. Increasing evidence has revealed that NLR is a simple, fast, and superior biomarker for predicting infection than leukocytes and CRP for emergency clinics, community-acquired infections [10,11].

In our retrospective study, the predictive value for SSI of peripheral WBCs and their subsets count and percentage, NLR at 1 week before the operation and at 4 and 7 days post-operation, and CRP at 4 and 7 days post-operation were assessed in 293 patients who underwent posterior lumbar spinal surgery.

2. Materials and methods

2.1. Study design

The study protocol was approved by the Ethics Committee of Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, China. This study initially retrospectively reviewed 1195 consecutive patients who underwent posterior lumbar spinal surgery for degenerative spine disease at the Department of Spine Surgery, TaiZhou Hospital of Zhejiang Province, China, from December 2016 to November 2018. All patients' medical history and the evidence for deep SSI were reviewed.

Deep SSI was determined according to criteria released by the U.S. Centers for Disease Control and Prevention [12]. A deep SSI was confirmed only when the surgeon diagnosed deep SSI and conducted debridement and positive microbiological culture. However, patients with existing infection including superficial SSI (n = 12), trauma, chronic inflammatory disease, and previous surgery of the lumbar spine were excluded from the study.

Among 1195 patients who underwent posterior lumbar spinal surgery, there were 13 patients with SSI, and laboratory data from 280 consecutive non-SSI patients were retrieved as the control group. Routine laboratory data including WBCs and their subsets count and percentage, NLR at 1 week before the operation and at 4 and 7 days post-operation, and CRP at 4 and 7 days post-operation were collected and analysed. Patient demographic and references of the related laboratory data are listed in Table 1. Reference intervals for blood cell analysis and the cut-off for CRP are according to the National Standard of the People's Republic of China WS/T 405–2012 and WS/T 404.9–2018, respectively. Normal reference intervals for NLR were as reported by Luo et al. [13] .

2.2. Statistical analysis

All statistical analyses between the SSI and non-SSI groups were performed by SPSS 13.0 (SPSS, Inc., Chicago, IL). Quantitative variables such as age, operating time, length of stay, WBCs and their subsets count and percentage, NLR and CRP were analysed with the Mann–Whitney *U* test. Qualitative variables such as patient sex, status of hypertension and diabetes were analysed by χ^2 test with Fisher's exact probability. Receiver operating characteristics (ROC) analysis was performed for variables between the SSI and non-SSI groups, and the cut-off value including the sensitivity and specificity of related variables was determined by Youden's index. All statistical analyses were two-sided and $p < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of demographic and laboratory data between SSI and non-SSI patients

Among these patients, 13 SSI patients were identified in the study. The microbiological culture results for patients with SSI are shown in Table 2, and the timeline of onset of infection in days after the operation in SSI patients are shown in Fig. 1.

Demographic data analysis showed that no significant difference was observed for patient age, sex, operation time, status of hypertension and diabetes between the SSI and non-SSI patients; however, the length of hospital stay was much longer in SSI compared to in non-SSI patients (37.0 days vs 14.0 days; $p < 0.001$), which could have resulted from more medical treatments for the SSI patients.

Analysis of laboratory data at 4 days post-operation revealed that the median percentage of neutrophils (77.2% vs 71.8%; $p = 0.010$) and NLR (5.40 vs 3.69; $p = 0.011$) were markedly increased and the median percentage of leukocytes were dramatically decreased (14.80 vs 19.20; $p = 0.027$) in the SSI group compared to that in the non-SSI group. In contrast, there were no obvious differences in total WBC count ($p = 0.282$) or neutrophil ($p = 0.121$), leukocyte ($p = 0.124$), and CRP levels ($p = 0.447$) between the two groups. Analysis of laboratory data at 7 days post-operation showed that the median neutrophil count (7.1×10^9/L vs 4.9×10^9/L; $p = 0.039$), percentage (73.7% vs 68.3%; $p = 0.030$) and NLR (4.3 vs 3.2; $p = 0.047$) were markedly increased in the SSI group compared to that in the non-SSI group, while there were no obvious differences in other laboratory parameters between the two groups (Table 1). The distribution of each of the variables at 4 and 7 days post-operation are presented in Fig. 2 and Fig. 3. However, no significant difference was observed between the SSI and non-SSI groups at 1 week before the operation (Suppl. Fig. 1).

In addition, data revealed that the NLR at 4 days post-operation was significantly higher in the SSI patients infected with gram-negative bacteria compared to that of patients infected with gram-positive bacteria ($p = 0.003$; Fig. 4).

3.2. ROC and logistic regression analysis of 4 and 7 days post-operative NLR between SSI and non-SSI patients

ROC curve analysis showed that both the 4 and 7 days post-operative NLR levels could effectively distinguish SSI patients from non-SSI patients. The area under the curve (AUC) for the 4 days post-operative NLR was 0.708 (95% CI: 0.543–0.837; $p = 0.021$; Fig. 5A), and the 7 days post-operative NLR was 0.663 (95% CI: 0.521–0.806; $p = 0.047$; Fig. 5B), respectively. For other parameters, the AUC for the percentages of neutrophils and lymphocytes at 4 days post-operation was 0.713 ($p = 0.010$) and 0.682 ($p = 0.027$; Suppl. Fig. 2A and B), respectively, and the percentage and count of neutrophils at 7 days post-operation was 0.678 ($p = 0.030$) and 0.669 ($p = 0.039$; Suppl. Fig. 2C and D), respectively.

Then, the optimal cut-off value for the variables was determined according to Youden's index (J = sensitivity + specificity-1) with maximum value. Data showed that an optimal cut-off value for the 4 days post-operative NLR was 5.19 (sensitivity: 61.5%; specificity:77.6%), and the optimal cut-off value for the 7 days post-operative NLR was 3.85 (sensitivity: 69.2%; specificity: 62.7%).

Finally, whether the 4 and 7 days post-operative NLR were valuable laboratory predictors for SSI were analysed by logistic regression model. Data showed that NLR at both post-operative time points (OR = 1.218; $p = 0.003$ and OR = 1.296; $p = 0.048$) could be valuable predictors for SSI (data not shown).

4. Discussion

Surgical site infection (SSI) is one of the serious complications in

Table 1
Patient demographic and laboratory data.

Variables	Reference	SSI (n = 13) Median (range)	Non-SSI (n = 280) Median (range)	*p*
Age (yr)	/	62 (44–72)	61 (34–98)	0.510
Sex (male/female)	/	8/5	144/136	0.911
Operating time (min)	/	167 (85–234)	155 (45–422)	0.717
Hypertension (No/Yes)	/	9/4	188/92	0.875
Diabetes (No/Yes)	/	11/2	252/28	0.531
Length of stay (days)	/	37.0 (12–160)	14 (5–59)	< 0.001
4 days post-operation				
WBC (10^9/L)	3.5–9.5	10.3 (3.5–15.1)	7.8 (3.5–17.6)	0.282
Neutrophil (10^9/L)	1.8–6.3	7.0 (3.0–13.8)	5.5 (0.8–15.1)	0.121
Lymphocyte (10^9/L)	1.1–3.2	1.2 (0.3–2.9)	1.5 (0.3–3.6)	0.124
Neutrophil (%)	40.0–75.0	77.2 (60.8–91.6)	71.8 (50.4–93.5)	0.010
Lymphocyte (%)	20.0–50.0	14.8 (5.4–28.3)	19.2 (3.9–42.2)	0.027
NLR	0.88–4.0	5.4 (2.1–17.30)	3.69 (0.87–23.6)	0.011
CRP (mg/L)	< 6.0	49.9 (4.1–130.9)	40.4 (0.6–253.0)	0.447
7 days post-operation				
WBC (10^9/L)	3.5–9.5	8.9 (4.2–19.0)	7.3 (3.3–18.2)	0.099
Neutrophil (10^9/L)	1.8–6.3	7.1 (2.6–15.3)	4.9 (1.7–15.4)	0.039
Lymphocyte (10^9/L)	1.1–3.2	1.3 (0.9–2.9)	1.5 (0.5–4.1)	0.559
Neutrophil (%)	40.0–75.0	73.7 (62.5–71.7)	68.3 (40.5–86.8)	0.030
Lymphocyte (%)	20.0–50.0	18.1 (9.0–26.9)	20.8 (8.4–44.0)	0.073
NLR	0.88–4.0	4.3 (2.4–8.7)	3.2 (0.9–10.0)	0.047
CRP (mg/L)	< 6.0	36.8 (16.5–104.0)	32.3 (0.5–162.6)	0.140

Table 2
Microbiological culture data in the SSI group.

No.	Age	Sex	Diabetes	Hypertention	Culture
1	45	Male	No	No	Kebsiella pneumoniae
2	69	Male	No	Yes	*Staphylococcus epidermidis*
3	44	Female	No	No	Staphylococcus epidermidis
4	48	Male	No	No	Staphylococcus capitis
5	72	Female	Yes	Yes	Unknown
6	57	Male	No	No	Acinetobacter baumannii
7	61	Male	No	No	Staphylococcus epidermidis
8	65	Female	No	Yes	Acinetobacter baumannii
9	50	Male	No	No	*Enterobacter aerogenes*
10	68	Female	Yes	Yes	Staphylococcus epidermidis
11	62	Female	No	No	*Staphylococcus aureus*
12	63	Male	No	No	Staphylococcus aureus
13	69	Male	No	No	Acinetobacter baumannii

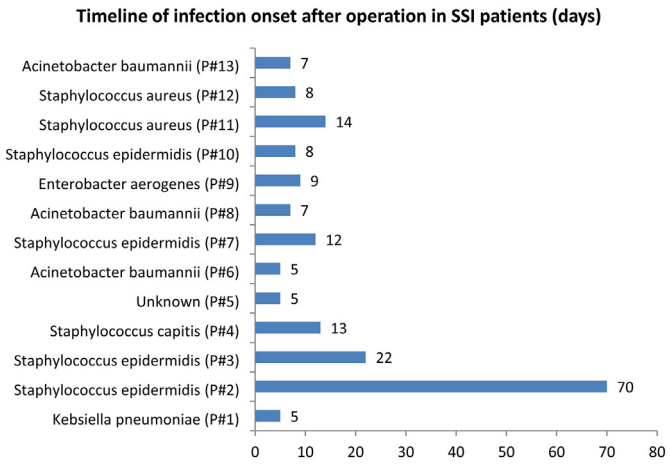

Fig. 1. Timeline of onset of infection in days after operation in individual SSI patients with the infected bacteria.

patients after posterior lumbar surgery. Many risk factors associated with the incidence of SSI have been proposed and various prophylaxis measures have been taken to prevent the occurrence of SSI [14]. Moreover, screening and diagnosis of early SSI with potential laboratory markers such as CRP, ESR and count and/or percentage of WBCs and their subsets (due to their objectivity, low cost, convenience and non-invasiveness), has received interest in recent years [15].

As early as 2006, Takahashi et al. [16] first analysed the kinetics of lymphocytes in patients who underwent spinal instrumentation surgery, although the cohort size was very limited. They reported that WBCs and the percentage and number of neutrophils increased, while the percentage and number of lymphocytes decreased at 4 days post-operation in patients with SSI. Since then, a number of studies have been carried out to focus on the clinical significance of count and percentage of WBCs and their subsets and have derived indices such as NLR and platelet-to-lymphocyte ratio (PLR) which now have been investigated in the early diagnosis of SSI in patients after spine and other surgical operations [17,18]. In this context, a study by Iwata et al. [19] showed that an increased CRP level and a decreased lymphocyte count at 4 days post-operation could be useful screening items for SSI in patients who underwent posterior lumbar spinal surgery. Their recent study further revealed that a decreased percentage and count of lymphocytes at 4 days post-operation, which was unaffected by operative factors, could be a reliable screening laboratory marker for SSI after posterior lumbar decompression surgery [20]. In that study, the cutoff for the percentage of lymphocyte at 4 days post-operation was < 19.4% (sensitivity: 80.0%; specificity: 62.5%; AUC: 0.708). In our study, similar data were obtained, and the percentage of lymphocytes at 4 days post-operation was significantly decreased in SSI patients. When the cutoff < 15%, the sensitivity was 61.5%, and specificity was 73.3% (AUC = 0.682) at the 4 days post-operation. We also found that the percentage of neutrophils at both 4 and 7 days post-operation could discriminate the SSI and non-SSI groups with an AUC of 0.713 (p = 0.010) and 0.678 (p = 0.030), respectively.

To be noted, increasing evidence has emphasized that NLR is a simple and even better marker than CRP for predicting infection as reported in patients with burn injuries or using domiciliary non-invasive mechanical ventilation [21,22]. Interestingly, NLR was the only marker that was dramatically significant in patients with *E. coli* urinary tract infections after renal transplantation [23]. However, the clinical significance of NLR in the prediction of SSI in spinal surgery remains to be investigated. In this study, our data presented that the NLR was much higher in SSI patients at both 4 and 7 days post-operation and could be a valuable indicator for SSI after posterior lumbar spinal

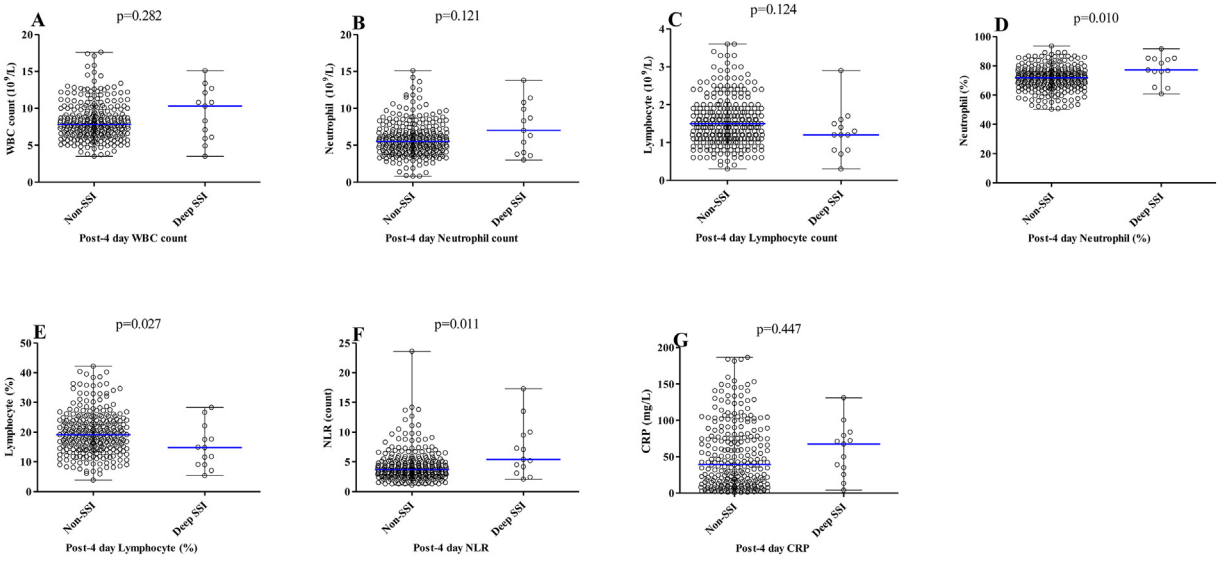

Fig. 2. The distribution and comparison of 4-days post-operative laboratory variables between the patients with SSI (n = 13) and non-SSI (n = 280) patients. (A) WBC count; (B) neutrophil count; (C) lymphocyte count; (D) percentage of neutrophils; (E) percentage of lymphocytes; (F) neutrophil/lymphocyte count ratio; and (E) CRP. The blue line represents the median values. All comparisons were performed with the Mann-Whitney *U* test. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

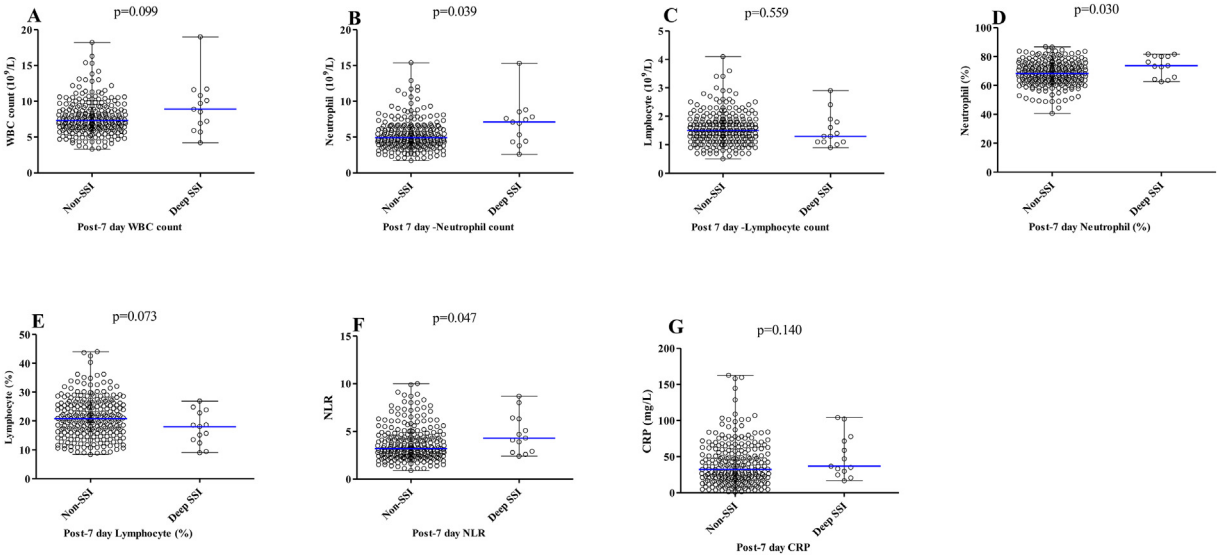

Fig. 3. The distribution and comparison of 7-days post-operative laboratory variables between the SSI (n = 13) and non-SSI (n = 280) patients. (A) WBC count; (B) neutrophil count; (C) lymphocyte count; (D) percentage of neutrophils; (E) percentage of lymphocytes; (F) neutrophil/lymphocyte count ratio; and (E) CRP. The blue line represents the median values. All comparison were performed with the Mann-Whitney U test. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

surgery. With the optimal NLR cutoff value > 5.19, the sensitivity was 61.5%, and the specificity was 77.6% (AUC = 0.708) at 4 days post-operation, and with the optimal NLR cut-off value is > 3.85, the sensitivity was 69.2% and specificity was 62.7% at 7 days post-operation. Interestingly, with the limited, small size sample of patients, our data revealed that the NLR at 4 days post-operation was significantly higher in SSI patients infected with gram-negative compared to that of patients infected with gram-positive bacteria ($p = 0.003$). However, the underlying mechanisms remain elusive and the findings obtained in previous studies are controversial. Vandijck et al. [24] reported that WBC count was dramatically increased in patients infected with gram-negative bacteria as compared to patients infected with gram-positive bacteria, while others documented that the WBC counts were not related to the types of infectious bacteria and their gram staining status [25,26]. Moreover, our data also showed that the neutrophil percentage was obviously elevated in SSI patients as compared to that in non-SSI patients both at 4 days and 7 days post-operation. As the logistic regression analysis indicated, the neutrophil percentage and NLR could be valuable predictors for SSI.

Our present study does have several limitations. First, due to the rare incidence of the SSI cases and their very limited sizes, only 13 patients with SSI were identified and included in the study. Second, this was a retrospective study and only three time points were included before and after the operation. Third, the follow-up period was relatively short and some patients who later developed SSI would be missed. Additionally, different operation procedures may alter the levels of the laboratory indices. Therefore, a multi-centre prospective study with a larger cohort and dynamic evaluation of the clinical laboratory parameters may help to solve these problems.

In summary, our findings indicated that the count and percentage of

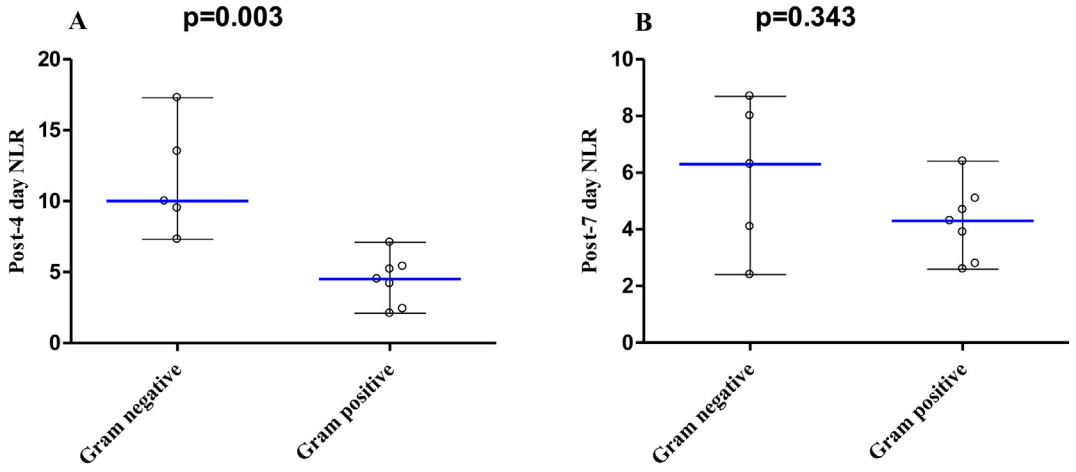

Fig. 4. Comparison of the NLR levels between the SSI patients infected with Gram negative (n = 5) bacteria and Gram positive (n = 7) bacteria at 4-days post-operation (A) and at 7-days post-operation (B).

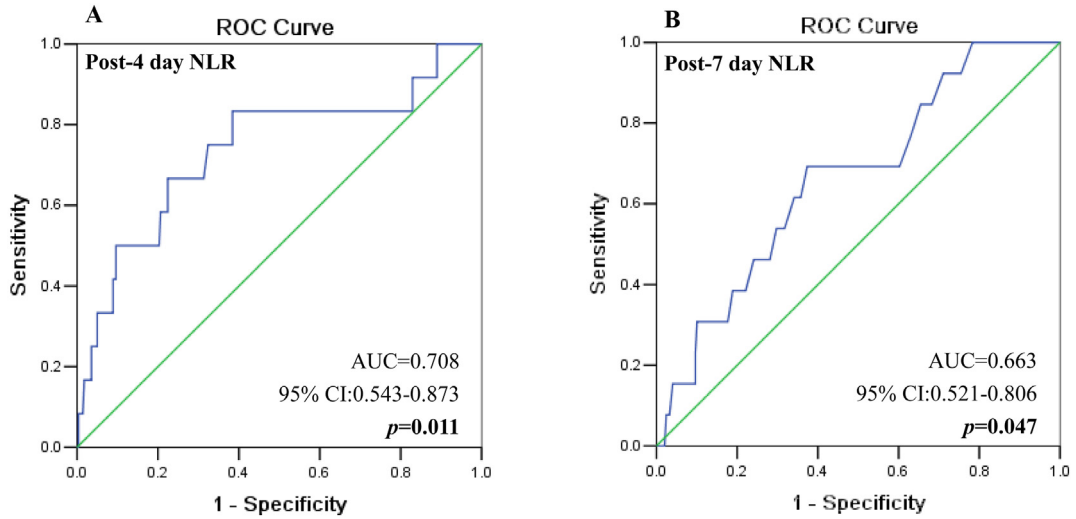

Fig. 5. ROC analysis for NLR in discriminating between SSI (n = 13) and non-SSI (n = 280) patients at 4 -days post-operation (A) and at 7 -days post-operation (B).

peripheral WBCs and their subpopulations are of importance in the screening of early SSI among patients after posterior lumbar spinal surgery, which might be valuable for the early diagnosis and control of infection. NLR at 4 and 7 days post-operation could be a predictor for SSI in patients undergoing posterior lumbar spinal surgery, which can be very convenient as these are routine laboratory tests and can help a physician to make treatment choices. However, a multi-centre prospective study with a larger cohort and dynamic evaluation of the clinical laboratory parameters may help to validate the significance of these parameters in predicting SSI in patients who underwent posterior lumbar spinal surgery.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.intimp.2019.105705.

Declaration of Competing Interest

The authors report no proprietary or commercial interest in any product mentioned or concept discussed in this article.

References

[1] T. Lan, S.Y. Hu, Y.T. Zhang, et al., Comparison between posterior lumbar interbody fusion and transforaminal lumbar interbody fusion for the treatment of lumbar degenerative diseases: a systematic review and meta-analysis, World Neurosurg. 112 (2018) 86–93.

[2] R. Yao, H. Zhou, T.J. Choma, et al., Surgical site infection in spine surgery: who is at risk? Global Spine J. 8 (4 Suppl) (2018) 5S–30S.

[3] S. Ogihara, T. Yamazaki, H. Inanami, et al., Risk factors for surgical site infection after lumbar laminectomy and/or discectomy for degenerative diseases in adults: a prospective multicenter surveillance study with registry of 4027 cases, PLoS One 13 (10) (2018) e0205539.

[4] J.M. Liu, H.L. Deng, X.Y. Chen, et al., Risk factors for surgical site infection after posterior lumbar spinal surgery, Spine (Phila Pa 1976) 43 (10) (2018) 732–737.

[5] D. Xing, J.X. Ma, X.L. Ma, et al., A methodological, systematic review of evidence-based independent risk factors for surgical site infections after spinal surgery, Eur. Spine J. 22 (3) (2013) 605–615.

[6] T. Makino, T. Kaito, H. Tsuboi, et al., Late-onset deep surgical-site infection after posterior lumbar interbody fusion in a patient treated with tocilizumab; unusual changes in inflammatory markers, Eur. Spine J. 23 (Suppl. 2) (2014) 296–301.

[7] H. Inanami, Y. Oshima, T. Iwahori, et al., Role of 18F-fluoro-D-deoxyglucose PET/CT in diagnosing surgical site infection after spine surgery with instrumentation, Spine (Phila Pa 1976) 40 (2) (2015) 109–113.

[8] E. Iwata, H. Shigematsu, M. Koizumi, et al., Lymphocyte count at 4 days post-operatively and CRP level at 7 days postoperatively: reliable and useful markers for surgical site infection following instrumented spinal fusion, Spine (Phila Pa 1976) 41 (14) (2016) 1173–1178.

[9] B.E. Broca-Garcia, M.A. Saavedra, M.A. Martinez-Bencomo, et al., Utility of neutrophil-to-lymphocyte ratio plus C-reactive protein for infection in systemic lupus erythematosus, Lupus 28 (2) (2019) 217–222.

[10] K. Westerdijk, K.S. Simons, M. Zegers, et al., The value of the neutrophil-lymphocyte count ratio in the diagnosis of sepsis in patients admitted to the Intensive Care Unit: a retrospective cohort study, PLoS One 14 (2) (2019) e0212861.

[11] V. Manohar, S.B. Prasad, S. Raj, et al., The eminence of neutrophil-lymphocyte count ratio in predicting bacteremia for community-acquired infections at an emergency medicine department in a tertiary care setting, J. Emerg. Trauma Shock 11 (4) (2018) 271–275.

[12] T.C. Horan, R.P. Gaynes, W.J. Martone, et al., CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections, Am. J. Infect. Control 20 (5) (1992) 271–274.
[13] H. Luo, L. He, G. Zhang, et al., Normal reference intervals of neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, lymphocyte-to-monocyte ratio, and systemic immune inflammation index in healthy adults: a large multi-center study from Western China, Clin. Lab. 65 (3) (2019).
[14] N.T. Spina, I.S. Aleem, A. Nassr, et al., Surgical site infections in spine surgery: preoperative prevention strategies to minimize risk, Global Spine J. 8 (4 Suppl) (2018) 31S–36S.
[15] K.T. Kang, D.W. Son, S.H. Lee, et al., Variation of C-reactive protein and white blood cell counts in spinal operation: primary fusion surgery versus revision fusion surgery, Korean J. Spine 14 (3) (2017) 66–70.
[16] J. Takahashi, Y. Shono, H. Hirabayashi, et al., Usefulness of white blood cell differential for early diagnosis of surgical wound infection following spinal instrumentation surgery, Spine (Phila Pa 1976) 31 (9) (2006) 1020–1025.
[17] H.J. Son, J.L. Roh, S.H. Choi, et al., Nutritional and hematologic markers as predictors of risk of surgical site infection in patients with head and neck cancer undergoing major oncologic surgery, Head Neck 40 (3) (2018) 596–604.
[18] A. Frances Borrego, F.M. Martinez, et al., Diagnosis of infection in hip and knee revision surgery: intraoperative frozen section analysis, Int. Orthop. 31 (1) (2007) 33–37.
[19] E. Iwata, H. Shigematsu, M. Koizumi, et al., Lymphopenia and elevated blood C-reactive protein levels at four days postoperatively are useful markers for early detection of surgical site infection following posterior lumbar instrumentation surgery, Asian Spine J. 10 (2) (2016) 220–225.
[20] E. Iwata, H. Shigematsu, Y. Yamamoto, et al., Lymphocyte count at 4 days postoperatively: a reliable screening marker for surgical site infection after posterior lumbar decompression surgery, Spine (Phila Pa 1976) 43 (18) (2018) E1096–E1101.
[21] J. Fuss, A. Voloboyeva, V. Poliovyj, Prognostic value of using neutrophil-lymphocyte ratio in patients with burn injury for the diagnosis of sepsis and bacteraemia, Pol. Przegl. Chir. 90 (5) (2018) 13–16.
[22] B. Ocakli, E. Tuncay, S. Gungor, et al., Inflammatory markers in patients using domiciliary non-invasive mechanical ventilation: C reactive protein, procalcitonin, neutrophil lymphocyte ratio, Front. Public Health 6 (2018) 245.
[23] H. Kazimoglu, E. Uysal, M. Dokur, et al., Evaluation of the relationship between neutrophil lymphocyte ratio and the most common bacterial urinary tract infections after transplantation, Bratisl. Lek. Listy 120 (2) (2019) 161–165.
[24] D.M. Vandijck, E.A. Hoste, S.I. Blot, et al., Dynamics of C-reactive protein and white blood cell count in critically ill patients with nosocomial Gram positive vs. Gram negative bacteremia: a historical cohort study, BMC Infect. Dis. 7 (2007) 106.
[25] F. Ratzinger, M. Dedeyan, M. Rammerstorfer, et al., Neither single nor a combination of routine laboratory parameters can discriminate between Gram-positive and Gram-negative bacteremia, Sci. Rep. 5 (2015) 16008.
[26] R. Abe, S. Oda, T. Sadahiro, et al., Gram-negative bacteremia induces greater magnitude of inflammatory response than Gram-positive bacteremia, Crit. Care 14 (2) (2010) R27.