Preoperative lymphocyte percentage and neutrophil-lymphocyte ratio are useful predictors of 30-day postoperative complications after lumbar fusion

Temidayo Osunronbi1,2#, Balint Borbas3#, Hiba Lusta1, Agbolahan Sofela4, Himanshu Sharma4

1Department of Surgery, Hull University Teaching Hospitals NHS Trust, Anlaby Road, Hull, 2Department of Health Sciences, University of York, York, 3Peninsula Medical School, Faculty of Health, University of Plymouth, Plymouth Science Park, Plymouth, 4Southwest Neurosurgery Centre, University Hospitals Plymouth NHS Trust, Plymouth, United Kingdom.

E-mail: *Temidayo Osunronbi - temi.osunronbi@yahoo.co.uk; Balint Borbas - balint.borbas@nhs.net; Hiba Lusta - hiba.lusta@nhs.net; Agbolahan Sofela - agbolahan.sofela@nhs.net; Himanshu Sharma - himanshu.sharma@nhs.net

#These authors contributed equally to this work.

ABSTRACT

**Background:** Lymphocyte percentage/count, platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) have shown prognostic significance in patients with cancer, stroke, and following cardiac surgery. However, the utility of these blood parameters for assessing the 30-day postoperative risk for lumbar fusion complications has not been established.

**Methods:** In this single-center-single-surgeon retrospective series, 77 consecutive patients underwent one- or two-level lumbar fusion. Lymphocyte percentage/count, PLR, and NLR were investigated as predictors of 30-day postoperative complications.

**Results:** Ten of 77 patients had postoperative complications. A unit increase in NLR and lymphocyte percentage was significantly associated with a 23% increase and 7% decrease, respectively, in the odds of a complication occurring. Preoperative NLR ≥ 2.32 and lymphocyte percentage ≤ 29.5% significantly discriminated between the “complication” and “no-complication” groups.

**Conclusion:** Patients with a preoperative lymphocyte percentage of ≤29.5% and/or NLR ≥2.32 should be closely monitored as high-risk groups susceptible to 30-day postoperative complications after lumbar fusion.

**Keywords:** Complications, Lymphocyte, Neutrophil, Prognosis, Spinal fusion

INTRODUCTION

The importance of preadmission/preoperative lymphocyte percentage/count, platelet-lymphocyte ratio (PLR), and neutrophil-lymphocyte ratio (NLR) as prognostic markers following cardiac surgery, stroke, and cancers has been extensively reported.[14,48] Some spine surgery studies have also reported that lymphocyte count/percentage and NLR levels obtained between 3 and 7 days postoperatively helped predict whether surgical site infections (SSIs) would occur within 30 postoperative days.[2,17] Here, we investigated whether preoperative lymphocyte percentage/count, PLR, and NLR are useful predictors for 30-day postoperative complications following lumbar fusion.
MATERIALS AND METHODS

Study design

In this case–control study, 77 adults underwent elective single- (37 patients) or two-level (40 patients) posterior/posterolateral lumbar fusion performed by one surgeon (2012–2019) [Tables 1 and 2].

Statistical analysis

Statistical analysis was performed on IBM SPSS Statistics 27 (Windows). Binary logistic regression, receiver operating characteristics, and Youden’s index were utilized [Table 3].

RESULTS

Correlation between 30-day postoperative complications and lymphocyte percentage and NLR

Table 4 is a summary of the patients’ baseline characteristics. Postoperative complications occurred in 10 out of 77 patients (13%); three developed SSI, three pneumonia, and one with each of the following: atelectasis, gastroenteritis, peritonitis, and transient ischemic attack [Figure 1]. A unit increase in NLR and lymphocyte percentage was significantly associated with a 23% increase and 7% decrease, respectively, in the odds of a complication occurring. There were no statistically significant associations between the occurrence of complications and the other independent variables [Figure 2 and Table 5].

Predictive value of preoperative lymphocyte percentage and NLR for determining 30-day postoperative complications

The area under the curve values for the preoperative NLR and lymphocyte percentage were in the “acceptable” range (0.7–0.8) of prognostic accuracy for postoperative 30-day complications. The optimal cutoff value for preoperative NLR and lymphocyte percentage were ≥2.32 and ≤29.5%, respectively [Figure 3]. Compared to others, patients with a preoperative NLR ≥2.32 and those with a lymphocyte percentage ≤29.5% had 5.6 times and 13.9 times greater odds of postoperative complications, respectively [Figure 4].

Table 1: Inclusion and exclusion criteria.

| Inclusion criteria                  | Exclusion criteria                  |
|------------------------------------|-------------------------------------|
| Adult patients (≥18 years old)     | History of previous lumbar spine surgery |
| Posterior/posterolateral lumbar fusion | Three- or more level fusion          |
| Single- or two-level fusion        | History of hematological disorders  |
| Elective cases                     | Emergency cases                     |

Table 2: Summary of variables investigated.

| Demographic variables | Age | Sex | Smoking status | Body mass index | Charlson comorbidity index |
|-----------------------|-----|-----|----------------|-----------------|---------------------------|
| Perioperative variables | Neutrophil-lymphocyte ratio (NLR: neutrophil count÷lymphocyte count) | Spinal surgical levels |
| Laboratory variables   | Lymphocyte percentage (lymphocyte count x 100÷white cell count) | Lymphocyte count |
|                        | Platelet-lymphocyte ratio (PLR: platelet count÷lymphocyte count) | Acute kidney injury, arrhythmia, atelectasis, coma, death, deep vein thrombosis, delirium, electrolyte imbalance, epidural hematoma, gastrointestinal infection, ileus, myocardial infarction, new neuropathic pain, sepsis, surgical site infection, permanent peripheral nerve injury, peritonitis, pneumonia, pulmonary embolism, stroke, transient ischemic attack, urinary retention, and urinary tract infection |

Table 3: Statistical tests utilized at a 5% significance level with the occurrence of 30-day complications as the outcome measure.

| Test | Statistical test     | Independent variables                                                                 | Purpose                                                                 |
|------|----------------------|----------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| 1    | Binary logistic regression | Demographic, surgical, and laboratory parameters as listed in [Table 2] | To evaluate the association between the independent variables and the development of complications |
| 2a   | Receiver operating characteristics | The variables that were statistically significant in test 1 (i.e., NLR and lymphocyte percentage) | To determine the area under the curve for the variables in predicting complications |
| 2b   | Youden's index      | The variables that were statistically significant in test 1 (i.e., NLR and lymphocyte percentage) | To determine the optimal cutoff values, sensitivity, and specificity of the tested variables in predicting postoperative complications |
| 3    | Binary logistic regression | Dichotomized NLR and lymphocyte percentage derived from the cutoff values obtained in test 2b | To further estimate the association between NLR and lymphocyte percentage (dichotomized by cutoff values) and the occurrence of complications |
Figure 1: Incidence and types of postoperative complications (n = 77). SSI: Surgical site infection, TIA: Transient ischemic attack.

Figure 2: Odds ratio with 95% confidence interval for the occurrence of complications within 30 days after lumbar fusion according to demographic/surgical/laboratory parameters. a compared to female, b compared to nonsmokers, c compared to two-level fusion. *Statistically significant.

Table 4: Patient demographic and operative data.

| Variables (n=77) |   |
|-----------------|---|
| Age (years)     | 54.5±14.5 |
| Sex (female/male)| 44/33    |
| Smoker (yes/no) | 9/68     |
| Body mass index (kg/m^2) (n=66) | 28.9±4.8 |
| Charlson comorbidity index | 2.8±2.6 |
| Number of spinal levels operated | 37 |
| Neutrophil-lymphocyte ratio (n=71) | 2.76±2.57 |
| Lymphocyte percentage (%) (n=71) | 29.7±10.5 |
| Lymphocyte count (10^9/L) (n=71) | 2.1±0.7 |
| Platelet-lymphocyte ratio (n=71) | 136.5±46.0 |

*Statistically significant.

DISCUSSION

We investigated the preoperative predictors of postoperative complications after lumbar fusion. Patients with preoperative lymphocyte percentage ≤29.5% and/or NLR ≥ 2.32 had a higher risk of developing postoperative complications. Other studies have reported similar findings (i.e., high baseline/preoperative NLR and lymphocytopenia were predictors of worse outcomes).[1,4-6,8] Nevertheless, spine surgery biomarker studies found no statistically significant association between preoperative NLR or lymphocyte count/percentage and the development of postoperative SSI [Table 6].[27] These contradictory results, as we observed in our study, could be because preoperative NLR and lymphocyte percentage predicted the development of any complication but not specifically SSI. High NLR and/or decreased lymphocyte percentage may reflect an activated immune system and a heightened systemic inflammatory response to operative...
### Table 5: Odds ratio for the occurrence of complications within 30 days after lumbar fusion surgery.

| Variables                              | Complications | \( \text{Yes}^a (n=10) \) | \( \text{No}^a (n=67) \) | Odds ratio (95% CI) | \( P\text{-value}^b \) |
|----------------------------------------|---------------|----------------------------|---------------------------|---------------------|-------------------------|
| Age (years)                            |               | 48.2±19.1                  | 55.5±13.6                 | 0.97 (0.93–1.01)    | 0.145                   |
| Sex                                    |               |                            |                           |                     |                         |
| Male                                   |               | 5                          | 28                        | 1.39 (0.37–5.27)    | 0.626                   |
| Female                                 |               | 5                          | 39                        | 1.00 (reference)    |                         |
| Smoker                                 |               |                            |                           |                     |                         |
| Yes                                    |               | 2                          | 7                         | 2.14 (0.38–12.16)   | 0.390                   |
| No                                     |               | 8                          | 60                        | 1.00 (reference)    |                         |
| Body mass index (kg/m\(^2\))          |               | 31.1±7.3                   | 28.6±4.5                  | 1.12 (0.93–1.35)    | 0.246                   |
| Charlson comorbidity index             |               | 1.2±1.3                    |                           | 0.82 (0.49–1.37)    | 0.445                   |
| Number of spinal levels                |               |                            |                           |                     |                         |
| 1                                      |               | 4                          | 33                        | 0.69 (0.18–2.66)    | 0.586                   |
| 2                                      |               | 6                          | 34                        | 1.00 (reference)    |                         |
| Neutrophil-lymphocyte ratio            |               | 4.4±3.9                    | 2.5±2.2                   | 1.23 (1.002–1.51)   | 0.048*                  |
| Lymphocyte percentage (%)              |               | 23.2±13.2                  | 30.7±9.7                  | 0.93 (0.87–0.997)   | 0.040*                  |
| Lymphocyte count (10\(^9\)/L)         |               | 1.8±0.9                    | 2.2±0.7                   | 0.47 (0.17–1.31)    | 0.151                   |
| Platelet-lymphocyte ratio              |               | 144.0±37.1                 | 135.3±47.4                | 1.00 (0.99–1.02)    | 0.579                   |

\(^a\)Presented as absolute numbers for categorical variables and mean±standard deviation for quantitative variables; \(^b\)\( P\)-value determined by binary logistic regression; *statistically significant at 5% significance level

### Table 6: Summary of selected literature on the prognostic value of preoperative NLR and/or lymphocyte percentage.

| S. No. | Authors                  | Type of study | Sample size | Study population                                                                 | Primary outcome measures | Findings                                                                 | Method to define normal NLR |
|--------|--------------------------|---------------|-------------|----------------------------------------------------------------------------------|--------------------------|--------------------------------------------------------------------------|-----------------------------|
| 1      | Diem et al\(^1\)         | Retrospective | 52          | Patients with metastatic nonsmall-cell lung cancer treated with nivolumab        | OS                       | Preoperative NLR >6.5 was significantly associated with reduced OS       | Tertiles                    |
| 2      | Inose et al\(^2\)        | Retrospective | 254         | Patients undergoing spinal decompression surgery                                | SSI                      | No association between SSI and preoperative NLR or lymphocyte percentage | N/A                         |
| 3      | Kakhki et al\(^4\)       | Retrospective | 180         | Patients admitted with acute stroke                                             | Infection                | Preoperative NLR >5 is associated with a significant risk of pneumonia but not UTI or sepsis after a cerebral vascular event | Arbitrary                   |
| 4      | Manuel et al\(^5\)       | Retrospective | 141         | Pediatric patients undergoing the bidirectional Glenn procedure                 | Length of hospital stay (LOS) | Preoperative NLR >2 was significantly associated with increased LOS       | Arbitrary                   |
| 5      | Manuel et al\(^6\)       | Retrospective | 116         | Pediatric patients undergoing tetralogy of Fallot repair                        | AKI                      | Preoperative NLR >0.93 was significantly associated with Grade III AKI    | ROC analysis               |
| 6      | Shen et al\(^7\)         | Retrospective | 293         | Patients undergoing posterior lumbar spinal surgery                             | SSI                      | No association between SSI and preoperative NLR or lymphocyte percentage | N/A                         |

OS: Overall survival, SSI: Surgical Site Infection, AKI: Acute kidney injury
stress. This increases intraoperative cytokines that release damaging oxygen-derived free radicals, contributing to worse outcomes.[5,8]

CONCLUSION

A raised NLR (≥2.32) and/or decreased lymphocyte percentage (≤29.5%) at baseline predict the development of postoperative complications after lumbar fusion.

Declaration of patient consent

Patient’s consent not required as patients identity is not disclosed or compromised.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Diem S, Schmid S, Krapf M, Flatz L, Born D, Jochum W, et al. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as prognostic markers in patients with non-small cell lung cancer (NSCLC) treated with nivolumab. Lung Cancer 2017;111:176-81.
2. Inose H, Kobayashi Y, Yuasa M, Hirai T, Yoshii T, Okawa A. Postoperative lymphocyte percentage and neutrophil-lymphocyte ratio are useful markers for the early prediction of surgical site infection in spinal decompression surgery. J Orthop Surg 2020;28:2309499020918402.
3. Iwata E, Shigematsu H, Okuda A, Morimoto Y, Masuda K, Nakajima H, et al. Lymphopenia at 4 days postoperatively is the most significant laboratory marker for early detection of surgical site infection following posterior lumbar instrumentation surgery. Asian Spine J 2016;10:1042-6.
4. Kakhki RD, Dehghanei M, ArefNezhad R, Motedayyen H. The predicting role of neutrophil lymphocyte ratio in patients with acute ischemic and hemorrhagic stroke. J Stroke Cerebrovasc Dis 2020;29:105233.
5. Manuel V, Miana LA, Guerreiro GP, Tenório DF, Turquetto A, Penha JG, et al. Prognostic value of the preoperative neutrophil-lymphocyte ratio in patients undergoing the bidirectional Glenn procedure. J Card Surg 2020;35:328-34.
6. Manuel V, Miana LA, Turquetto A, Guerreiro GP, Fernandes N, Jatene MB. The role of the neutrophil-lymphocyte ratio for pre-operative risk stratification of acute kidney injury after tetralogy of Fallot repair. Cardiol Young 2021;31:1009-14.
7. Shen CJ, Miao T, Wang ZF, Li ZF, Huang LQ, Chen TT, et al. Predictive value of post-operative neutrophil/lymphocyte count ratio for surgical site infection in patients following posterior lumbar spinal surgery. Int Immunopharmacol 2019;74:105705.
8. Wu X, Luo Q, Su Z, Li Y, Wang H, Yuan S, et al. Prognostic value of preoperative absolute lymphocyte count in children with tetralogy of fallot. J Am Heart Assoc 2021;10:e019098.

How to cite this article: Osunronbi T, Borbas B, Lusta H, Sofela A, Sharma H. Preoperative lymphocyte percentage and neutrophil-lymphocyte ratio are useful predictors of 30-day postoperative complications after lumbar fusion. Surg Neurol Int 2022;13:145.