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ORIGINAL RESEARCH

Neutrophil-to-Lymphocyte Ratio as a Prognostic Marker for Hospital-Acquired Infections in Neurosurgical Patients

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Purpose: The neutrophil-to-lymphocyte ratio (NLR) is an inflammatory marker associated with adverse outcomes, including hospital-acquired infections (HAIs) and mortality. This study evaluated its prognostic value in neurosurgical patients.

Patients and Methods: In this retrospective study of 5474 neurosurgical admissions, 147 HAIs occurred in 93 patients (HAIs group). A control group of 181 patients was matched for age, sex, and mortality status. Clinical (Nutrition Risk Screening 2002 [NRS-2002], Glasgow Coma Scale [GCS]) and demographic variables were compared with NLR. Survival was analyzed using Kaplan–Meier curves. Statistical tests included chi-square, Mann–Whitney, ANOVA, log-rank.

Results: Patients with HAIs (58.1% male, mean age 63.7 ± 15.5 years) more often had malnutrition risk (NRS ≥ 3: 65.6% vs 11.0%, $p < 0.001$) and severe neurological impairment (GCS 3–8: 31.2% vs 8.8%, $p < 0.001$) than controls. Median length of hospital stay was longer in HAIs (40 vs 5.4 days, $p < 0.001$). Mean NLR was higher in HAIs (9.25 ± 6.11) than controls (7.99 ± 5.21, $p = 0.0001$), peaking at 12.78 in patients with central nervous system tumors. An NLR ≥ 17.7 predicted in-hospital mortality with 57.1% sensitivity and 89.4% specificity. In controls, mortality increased significantly above this threshold ($\chi^2 = 14.83$, $p = 0.00012$), whereas in HAIs the association was not significant. NLR was not linked to hospital stay.

Conclusion: NLR is a cost-effective marker predicting in-hospital mortality in neurosurgical patients without HAIs, with ≥ 17.7 identifying high-risk cases. Its prognostic value in HAIs is limited and requires multicenter validation.

Keywords: neurosurgery, inflammatory biomarkers, hospital-acquired infection, prognosis, survival analysis

Introduction

The neutrophil-to-lymphocyte ratio (NLR), calculated from standard complete blood counts, has emerged as a widely studied indicator of systemic inflammation and immune dysregulation.[1] It reflects the balance between innate and adaptive immune responses, with elevated values observed in infection, trauma, malignancy, and cardiovascular disease.[2] Its ease of calculation, low cost, and availability from routine laboratory panels make NLR a potentially valuable clinical biomarker.[3]

Among inflammatory biomarkers, C-reactive protein (CRP) and procalcitonin (PCT) are the most commonly used in clinical practice for infection detection and monitoring.[4,5] CRP is sensitive but non-specific, as its concentration may increase in numerous inflammatory and non-infectious conditions.[4] PCT demonstrates greater specificity for bacterial infections and sepsis but is relatively costly, not universally available, and may vary depending on the timing of measurement and clinical context.[5] In contrast, NLR can be rapidly calculated from routine blood tests at no additional cost, making it a practical tool for repeated measurements and dynamic patient monitoring.[1,3,6] Therefore, NLR may complement, or in certain settings replace, CRP and PCT in the early identification of patients at risk for adverse outcomes.[4–6]

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Numerous studies have demonstrated the prognostic significance of NLR in various settings, including sepsis, ischemic stroke, traumatic brain injury, and postoperative complications.[7–10] In neurosurgery, elevated NLR has been associated with worse outcomes in patients with aneurysmal subarachnoid hemorrhage, brain tumors, and craniocerebral trauma.[11–13] For example, elevated NLR levels correlated with higher mortality and poorer neurological recovery after aSAH and more aggressive tumor behavior in patients with glioblastoma multiforme.[11,14] However, the literature remains heterogeneous, with different thresholds, timings of measurement, and clinical endpoints being evaluated.

Hospital-acquired infections (HAIs) are infections that develop during healthcare services and were not present at the time of admission; they can occur in a variety of healthcare settings and affect both patients and healthcare staff.[15] They are one of the greatest challenges facing healthcare today. In Europe, approximately 80,000 hospitalized patients suffer from at least one hospital-acquired infection every day, resulting in 16 million additional hospital days per year.[16] The incidence of HAIs in high-income countries averages 7.5%, while in low- and middle-income countries it ranges from 5.7% to 19.2%.[15,16] Despite the development and implementation of increasingly effective preventive measures, these infections cannot be completely prevented.[17]

Neurosurgical departments are recognized as high-risk settings for HAIs due to the complexity and specificity of procedures involving the central nervous system (CNS).[18–20] Available epidemiological data are limited, but studies estimate the incidence of HAIs in neurosurgical patients at 2–14%, with the highest rates observed among those requiring intensive care.[18–20] Brain injury—particularly in critically ill patients—is a major predisposing factor for infection.[20,21] Several mechanisms contribute to this increased susceptibility, including the severity of the underlying neurological condition, compromised immune responses, extensive use of invasive medical devices, prolonged hospitalization, and impaired consciousness.[20–23] A central component of care in severe CNS injury is the prevention of secondary brain damage, which is closely linked to minimizing infection risk.[24] Therefore, effective prevention and control strategies targeting HAIs are essential to improving outcomes in this patient group.[17,25]

Recent neurosurgical cohorts have also underscored the role of inflammatory indices in postoperative infection risk. Chen et al examined inflammatory markers and constructed a prediction model for postoperative pulmonary infection after aneurysmal subarachnoid hemorrhage,[26] while Pahwa et al reported predictors of neurosurgical postoperative infections in a retrospective analysis.[27]

Given these mechanisms, NLR has the potential to serve as a link between systemic inflammatory response and infection risk in neurosurgical patients.[1,3] Elevated postoperative NLR may not only indicate a heightened inflammatory state but also identify patients in whom immune dysregulation predisposes to HAIs.[1,3,6] Early identification of such high-risk patients could guide closer monitoring, timely antimicrobial intervention, and targeted infection prevention strategies.[17,25]

Despite these advantages, the prognostic value of NLR in neurosurgical patients with and without HAIs remains understudied. Moreover, its role as an independent predictor of in-hospital mortality, as well as its association with infection-specific outcomes, requires further clarification. Therefore, the aim of this study was to evaluate the prognostic significance of NLR in neurosurgical patients with and without hospital-acquired infections. We also sought to determine a clinically relevant NLR threshold predictive of in-hospital mortality.

Materials and Methods

This is a retrospective cross-sectional study conducted at a tertiary medical center, in accordance with the ethical principles of the Declaration of Helsinki (as amended in 2013). The study was approved by the host institution and the relevant bioethics committee (consent number 182/2022). Due to the retrospective design of the study, informed consent was waived, and all patient data were anonymized and de-identified. The study was conducted and reported in accordance with the RECORD (STROBE extension) guidelines.

Study Population

During the study period (2019–2023), 5474 patients were hospitalized, of whom 147 (2.7%) cases of hospital-acquired infections were identified in 93 patients (some patients had more than one infection). This cohort constituted the study group.

The inclusion criteria for the hospital-acquired infections group were as follows: patients hospitalized in the neurosurgery department for more than 48 hours[17] clinical picture consistent with infection or microbiological confirmation of hospital-

acquired infection, age over 18 years (our neurosurgery department admits only adults; pediatric neurosurgical cases are treated in a separate children's hospital).

Additionally, a control group of patients without hospital-acquired infections was included (hospitalization >48 hours; age ≥18 years). To increase statistical stability and reduce confounding, the control cohort was frequency-matched to the HAIs group on gender and age distribution. The final control sample comprised 40% women and 60% men, with the following age strata: 20–50 years (women 14%, men 16%), 51–60 (22%, 16%), 61–70 (16%, 26%), 71–80 (14%, 16%), and >80 (28%, 13%). To avoid imbalance in outcome prevalence, the overall in-hospital mortality proportion in controls was aligned at 16% (16%; 60% women, 40% men), with $p > 0.05$ for between-group comparisons. The flowchart is shown in Figure 1.

A total of 273 patients were included in the study: 93 with HAIs and 181 without HAIs. Both groups were comparable with respect to demographic characteristics. There were no significant differences between the groups in terms of gender, age, place of residence, or professional activity (all tests yielded $p > 0.05$).

Data Collection

Data for the study were obtained through a detailed analysis of the medical records of hospitalized patients, including medical histories, nursing histories, and materials developed by the Hospital Infection Team (infection charts). Data registration was performed by trained nurses after the patients were hospitalized, ensuring consistency and accuracy of information. For the purposes of the study, an original questionnaire was developed, divided into three sections:

- Sociodemographic and clinical data: including age, gender, place of residence, professional activity, diagnosis, assessment of nutritional status - NRS-2002 scale (Nutrition Risk Screening 2002)[28] and awareness - GCS scale (Glasgow Coma Scale).[29,30]
- Nosocomial infection risk assessment. An institutional, point-based admission form was used to quantify baseline risk of hospital-acquired infection. The tool consists of ten risk-factor categories: (1) age, (2) prior hospitalization within the past 12 months, (3) transfer from another healthcare facility, (4) diabetes mellitus, (5) other chronic comorbidities, (6) obesity, (7) malignancy, (8) immunosuppression, (9) cachexia, and (10) polytrauma. The cumulative score is mapped into five ordered strata: 0 (0 points), I (1–5), II (6–10), III (11–20), IV (>20), corresponding to very low, low, moderate, high, and very high risk, respectively. This 5-level variable is reported in Table 1 as the infection factor group and was used descriptively for baseline characterization; it was not included in multivariable models to avoid collinearity with its components and in view of incompletely captured individual comorbidity fields.

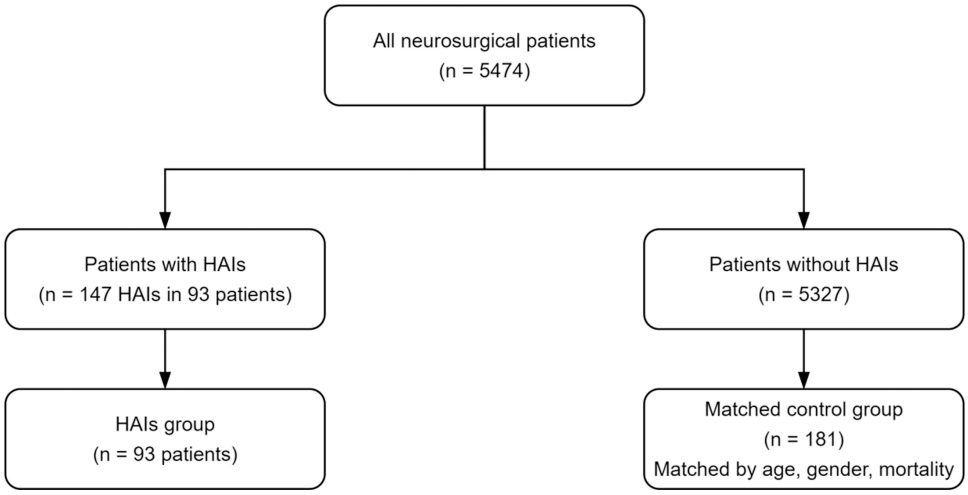

Figure 1 Patient selection flowchart. Among 5474 neurosurgical patients hospitalized between 2019 and 2024, 93 patients developed a total of 147 hospital-acquired infections (HAIs) and were included in the HAIs group. The control group (n = 181) was selected from 5327 patients without HAIs and matched by age, sex, and in-hospital mortality.

Abbreviation: HAIs, hospital-acquired infection.

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Table 1 Baseline Characteristics of Enrolled Patients

Variable	Total (n = 274)	HAIs group (n = 93)	Control group (n = 181)	Test statistic	P value	Effect size
Gender, n (%)				χ^2 = 0.240	0.620	φ = 0.029
Female	111 (40.1)	39 (41.9)	72 (39.8)			
Male	163 (59.9)	54 (58.1)	109 (60.2)			
Age, years, mean (SD)	64.63 (15.92)	63.72 (15.51)	65.55 (16.34)	*U* = 11939	0.140	*rg* = 0.114
Residence, n (%)				χ^2 = 0.336	0.540	φ = 0.035
Urban	123 (44.9)	73 (78.5)	50 (27.6)			
Rural	151 (55.1)	20 (21.5)	131 (72.4)			
Professional activity, n (%)				χ^2 = 1.220	0.270	φ = 0.066
Yes	72 (26.3)	26 (27.9)	46 (25.4)			
No	202 (73.7)	67 (72.0)	135 (74.6)			
Diagnosis, n (%)				χ^2 = 26.910	**0.001**	φ = 0.313
Craniocerebral trauma	82 (29.9)	35 (37.6)	47 (26.0)			
Cerebrovascular disease	78 (28.5)	26 (27.9)	52 (28.7)			
CNS tumors	84 (30.6)	24 (25.8)	60 (33.2)			
Other	30 (10.9)	8 (8.6)	22 (12.1)			
NRS-2002 score, n (%)				*U* = 4101	**<0.001**	*rg* = 0.660
< 3	192 (70.1)	32 (34.4)	160 (89.0)			
≥ 3	82 (29.9)	61 (65.6)	21 (11.0)			
GCS score, n (%)				*H* = 40.125	**<0.001**	ε^2 = 0.14
13–15 points	207 (75.5)	52 (55.9)	155 (85.6)			
9–12 points	22 (8.1)	12 (12.9)	10 (5.5)			
3–8 points	45 (16.4)	29 (31.2)	16 (8.8)			
Treatment, n (%)				χ^2 = 20.690	**<0.001**	φ = 0.274
Surgical	213 (77.7)	83 (89.2)	130 (71.8)			
Conservative	61 (22.2)	10 (10.8)	51 (28.2)			
Surgical procedure*, n (%)				χ^2 = 22.910	**<0.001**	φ = 0.289
Planned	126 (59.1)	35 (42.2)	91 (70.0)			
Urgent	87 (40.8)	48 (57.8)	39 (30.0)			
ASA score*, n (%)				*H* = 33.211	**<0.001**	ε^2 = 0.121
I	19 (8.9)	1 (1.2)	18 (7.7)			
II	50 (23.5)	14 (16.9)	36 (27.7)			
III	107 (50.0)	44 (53.0)	63 (48.5)			
IV	31 (14.6)	19 (22.9)	12 (9.2)			
V	6 (2.8)	5 (6.0)	1 (0.7)			
Infection factor group, n (%)				*H* = 23.166	**<0.001**	ε^2 = 0.121
0	8 (2.9)	8 (8.6)	0 (0.0)			
I	92 (33.6)	41 (44.1)	51 (28.2)			
II	62 (22.6)	18 (19.4)	44 (24.3)			
III	28 (10.2)	6 (6.5)	22 (12.2)			
IV	84 (30.7)	20 (21.5)	64 (35.3)			
Season, n (%)				χ^2 = 2.370	0.490	φ = 0.089
Spring	71 (25.9)	24 (25.8)	47 (26.0)			
Summer	85 (31.0)	29 (31.2)	56 (30.9)			
Autumn	66 (24.1)	21 (22.6)	45 (24.9)			
Winter	52 (19.0)	19 (20.4)	33 (18.2)			
Deaths, n (%)	40 (14.6)	15 (16.1)	25 (13.8)	χ^2 = 0.680	0.410	φ = 0.049
Average hospitalization time (days), mean (SD)	17.14 (31.51)	40.00 (45.77)	5.40 (5.29)	*U* = 9585	**<0.001**	*rg* = 0.880

- Data on treatment and hospitalization: analysis of type of therapy, type of surgery, ASA classification (American Society of Anesthesiologists Physical Status Classification System, ASA-PS),[31] season, length of hospitalization and treatment outcome (survival or death).

Comorbidity variables (eg, diabetes mellitus, chronic kidney disease, chronic immunosuppression) and procedure duration were not consistently available across the cohort and were therefore not included in the analyses.

Definitions and Measurements

Clinical signs of infection included fever, diarrhea, urinary or respiratory symptoms, and wound discharge. Trained nurses documented specific signs of infection. Laboratory and imaging results of all identified patients were reviewed and verified by a hospital microbiologist to confirm neurosurgery-specific infection criteria using CDC definitions (Centers for Disease Control and Prevention, a United States federal agency); HAIs in the neurosurgery unit were defined as those that occurred at least 48 hours after admission and were not present or evolving at the time of admission.[17]

For microbiological diagnosis of HAIs cases, appropriate clinical specimens (eg, blood, swabs, urine/stool samples, bronchoalveolar lavage (BAL), cerebrospinal fluid) were collected by nurses or physicians according to established procedures. For each HAIs, the infection subtype (respiratory, urinary tract, surgical-site, bloodstream, or CNS/meningitis–ventriculitis) and culture positivity (pathogen isolated: yes/no) were abstracted from Hospital Infection Team records according to CDC definitions, when available.

NLR was calculated as the absolute neutrophil count divided by the absolute lymphocyte count, derived from the first complete blood count (CBC) obtained on the day of hospital admission, prior to any neurosurgical procedure. By definition of HAIs ($\geq$ 48 h after admission), this baseline measurement necessarily preceded infection onset in the HAIs group. For descriptive analyses, NLR values $\leq$3 were classified as low and >3 as high.[10] Hematology testing was performed on automated analyzers (Sysmex XN-1000/XN-1500) using flow cytometry.

Statistical Analysis

Statistical analyses were performed using the Statistica 13.0 software package (TIBCO Software Inc., USA). Descriptive statistics (mean, standard deviation, median, interquartile range) were used to characterize the data distribution.

Group comparisons were conducted using appropriate parametric or non-parametric tests, depending on distribution shape and variable type. For continuous variables, ANOVA, Mann–Whitney U, or Kruskal–Wallis *H*-tests were used as appropriate. Categorical variables were analyzed using the Chi-square test or Fisher's exact test (in case of low cell counts). Correlations were assessed using Spearman's rank and tetrachoric correlation coefficients.

To validate survival patterns, Kaplan–Meier analysis was conducted with group stratification, and differences in survival were tested using Log rank test and Cox proportional hazards regression. To identify the prognostic threshold for mortality, ROC analysis was performed with cut-off selection based on the Youden index. To address the skewed and bimodal distribution of hospitalization time, a generalized linear model (GLZ) with a log link and normal distribution was fitted, including NLR and HAI status as predictors.

Although the large sample size met the assumptions of the central limit theorem, non-parametric and GLZ methods were chosen in selected analyses to better accommodate skewness and non-normality, particularly for hospitalization duration and clinical scales. To supplement p-values and enhance interpretability, effect sizes were calculated and reported where applicable: Φ (phi coefficient) for dichotomous or nominal variables (Chi-square), ε^2 (epsilon squared) for Kruskal–Wallis tests, η^2 (eta squared) for ANOVA, rg (rank-biserial correlation) for Mann–Whitney *U*-tests. Given limited events in some subgroups and small cell counts for certain comparisons, we prioritized estimation (effect sizes with 95% confidence intervals) over sole reliance on hypothesis testing and kept Cox models parsimonious in line with events-per-variable considerations.

The infection factor group was used descriptively for baseline characterization (Table 1) and was not entered into multivariable models to avoid collinearity with its components and because individual comorbidity fields were incompletely recorded.

Statistical significance was defined as $p < 0.05$. Values between 0.05 and 0.1 were interpreted as statistical trends. Newly added or revised tests and effect size measures were introduced after peer review to better reflect the magnitude of differences and increase analytical transparency.

Results

Patient Characteristics

In terms of demographic characteristics, such as gender, age, place of residence or professional activity, no statistically significant differences were observed between the groups ($p > 0.05$). Post hoc power calculations for the demographic comparisons are presented in the last column of Table 1, confirming adequate statistical power (>80%) for detecting moderate-to-large effect sizes in age and gender, while smaller differences may not have been detected. The HAIs group was dominated by men (58.1%), the mean age of patients was 63.72 ± 15.51 years, and the majority came from urban areas (78.5%). A similar distribution was observed in the control group (Table 1).

Hospital-acquired infections comprised pneumonia 25.9% (38/147), bloodstream infection 19.7% (29/147), surgical-site 16.3% (24/147), urinary tract 16.3% (24/147), CNS (meningitis/ventriculitis) 9.5% (14/147), gastrointestinal 8.8% (13/147), and other 3.4% (5/147). Among 192 microbiological isolates, Gram-negative organisms accounted for 50.0% (96/192), Gram-positive for 48.4% (93/192), and fungi for 1.6% (3/192); the most frequent species included *Staphylococcus aureus, Klebsiella pneumoniae, Escherichia coli*, and *Pseudomonas aeruginosa*. A compact summary of infection subtypes is provided in Table 2, and microbiological isolates are summarized in Table 2.

Table 2 HAIs Subtypes and Microbiology

HAIs subtypes (cases, N = 147)		
Subtype	**n**	**%**
Pneumonia	38	25.9
Bloodstream infection	29	19.7
Surgical-site infection	24	16.3
Urinary tract infection	24	16.3
CNS (meningitis/ventriculitis)	14	9.5
Gastrointestinal	13	8.8
Other	5	3.4
Total	**147**	**100**
Microbiological isolates (N = 192)		
Group	**n**	**%**
Gram-negative	96	50.0
Gram-positive	93	48.4
Fungi	3	1.6
Total	**192**	**100**

Note: Bolded p-values indicate statistical significance (<0.05). The p-value column reports values as x.xxx; values <0.001 are shown as <0.001. Effect sizes are reported to support interpretation. Variables marked with * apply only to surgically treated patients. Infection factor group corresponds to the institutional nosocomial infection risk assessment completed at admission; it summarizes ten risk-factor categories into five strata (very low–very high; coded 0–IV). This variable is used descriptively at baseline and was not entered into multivariable models (see Methods). Percentages may not sum to 100% due to rounding and polymicrobial episodes.

Abbreviations: HAIs, hospital-acquired infections; NRS-2002, Nutrition Risk Screening 2002; GCS, Glasgow Coma Scale; CNS, central nervous system; ASA, American Society of Anesthesiologists Physical Status Classification; SD, standard deviation; n, number of cases; %, percentage of subgroup; U, Mann–Whitney *U*-test statistic; χ^2, Pearson's chi-square test statistic; H, Kruskal–Wallis test statistic; p, significance level; φ, phi coefficient (categorical effect size); rg, rank-biserial correlation; ε^2, epsilon squared (Kruskal–Wallis effect size).

Analysis of diagnoses showed that patients from the HAIs group were significantly more often hospitalized due to craniocerebral injuries (37.6% vs 26.0%, $p < 0.001$). Other diagnoses, such as cerebrovascular diseases, CNS tumors, or other diseases, did not differ significantly between groups (Table 1).

Analysis of the clinical status of the patients showed that the HAIs group had more frequent features indicating a more severe course of the disease. In the NRS 2002 scale, 65.6% of patients from this group had a score of ≥ 3, compared with 11.0% in the control group ($p < 0.001$). In addition, the HAIs group had more patients with a severe clinical condition according to the GCS scale (3–8 points: 31.2% vs 8.8%, $p < 0.001$) and with a higher degree of surgical risk according to the ASA scale (ASA IV and V: 28.9% vs 9.9%, $p < 0.001$) (Table 1).

Surgical procedures were more common in the HAIs group, with 89.2% of patients undergoing surgical treatment compared with 71.8% in the control group ($p < 0.001$). Furthermore, acute procedures were significantly more common in the HAIs group (57.8% vs 30.0%, $p < 0.001$) (Table 1).

The mean duration of hospitalization in the HAIs group was 40 days, which was significantly longer compared to 5.4 days in the control group ($p < 0.001$) (Table 1).

The analysis of the number of deaths did not reveal any statistically significant differences between groups (16.1% vs 13.8%, $p > 0.05$) (Table 1).

Although patients in the HAIs group presented with more severe clinical status indicators (higher ASA and NRS-2002 scores, more frequent urgent surgeries, and prolonged hospitalization), the overall in-hospital mortality rate did not differ significantly between the HAIs and control groups (16.1% vs 13.8%, $p > 0.05$). This finding may reflect the multifactorial nature of mortality in neurosurgical patients, where outcomes are influenced not only by infection status but also by baseline neurological injury severity, comorbidities, and timely multidisciplinary care.

NLR Analysis and Demographic and Clinical Correlations

In the HAIs group, the mean NLR was 9.25, with a minimum value of 0.44 and a maximum of 43.4. In the control group, the mean NLR was 7.99, with a minimum value of 0.18 and a maximum of 94.4. The difference between the groups, assessed by the Mann Whitney ($U = 8018.5$, $p < 0.001$), was statistically significant (Table 3).

Table 3 Key Clinical Comparisons of NLR Between HAIs and Control Groups

Variable	HAIs Group (Mean ± SD)	Control Group (Mean ± SD)	Test	*P* value	Effect Size
NLR (overall)	9.25 ± 7.26	7.99 ± 10.83	$U = 8018.5$	**< 0.001**	**$rg = 0.261$**
Death: Deceased	7.90 ± 5.42	15.19 ± 14.75	$F = 6.410$	**0.001**	**$\eta^2 = 0.031$**
Death: Survived	9.58 ± 7.63	6.84 ± 9.63			
GCS: 13–15 pts	9.73 ± 8.01	6.60 ± 9.35	$F = 5.530$	**< 0.001**	**$\eta^2 = 0.04$**
GCS: 9–12 pts	8.23 ± 3.34	13.82 ± 9.87			
GCS: 3–8 pts	8.91 ± 7.10	17.89 ± 17.43			
ASA I	43.3 ± 0.00	3.99 ± 3.97	$F = 7.330$	**0.001**	**$\eta^2 = 0.18$**
ASA II	6.19 ± 3.77	5.42 ± 5.16			
ASA III	11.31 ± 8.29	7.58 ± 5.95			
ASA IV	6.75 ± 4.01	15.70 ± 16.60			
ASA V	9.27 ± 3.36	8.99 ± 0.00			
Surgery: Planned	9.66 ± 7.31	6.22 ± 4.99	$F = 3.65$	**0.010**	**$\eta^2 = 0.002$**
Surgery: Urgent	9.38 ± 7.62	9.64 ± 11.52			
Type of treatment: Surgical	9.48 ± 7.50	7.24 ± 7.68	$F = 1.610$	0.180	$\eta^2 = 0.002$
Type of treatment: Conservative	6.94 ± 3.50	9.92 ± 16.27			

Note: Group differences were tested with one-way ANOVA (F) or the Mann–Whitney *U*-test (U), as appropriate. Effect sizes are reported as η^2 for ANOVA and rg (rank-biserial correlation) for Mann–Whitney U. The p-value column reports values as x.xxx; values <0.001 are shown as <0.001. Bold indicates statistical significance (<0.05).

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; HAIs, hospital-acquired infections; GCS, Glasgow Coma Scale; ASA, American Society of Anesthesiologists.

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The mean NLR value for women in the HAIs group was 9.23, while for men it was 9.26. In the control group, women had a mean NLR value of 6.79, and men had a mean NLR value of 8.80. No significant difference was observed between the genders (F = 1.05, p = 0.37) (Table 4).

Age analysis showed that in the HAIs group, the highest NLR was observed in the age group of 36–45 years (M = 12.01), and the lowest in the age group of 26–35 years (M = 4.69). In the control group, the highest NLR was observed in the age group above 65 years (M = 9.58). The differences between the age groups were not statistically significant (H = 0.799, p = 0.63) (Table 4).

The highest NLR in the HAIs group was observed in patients with CNS tumors (malignant tumors: M = 11.82, benign tumors: M = 12.78) and brain injuries (M = 9.68). In the control group, the highest NLR was observed in patients with cerebral hemorrhage (M = 12.82) and subarachnoid hemorrhage (aneurysmal subarachnoid hemorrhage - aSAH) (M = 11.93). The lowest NLR values were observed in neuromuscular diseases and epilepsy (Table 4).

Further analysis of NLR values based on the NRS2002 score showed that for NRS < 3 the mean in the HAIs group was 8.92, while in the control group it was 7.37. For NRS ≥ 3 the mean in the HAIs group was 9.4, while in the control group it was 7.99. No statistically significant differences were observed (F = 2.44, p = 0.06) (Table 4).

NLR was also analyzed in terms of GCS. For patients with GCS scores of 12–9, the mean NLR in the HAI s group was 8.23 and in the control group 13.82, a difference that was statistically significant (p = 0.0001). For patients with GCS

Table 4 Supplementary Demographic and Contextual Comparisons of NLR

Variable	HAIs group (Mean ± SD)	Control group (Mean ± SD)	Test	P value	Effect size
Gender: Female	9.23 ± 6.49	6.79 ± 7.66	F = 1.050	0.370	η^2 < 0.01
Gender: Male	9.26 ± 7.88	8.80 ± 12.46			
Age: 18–25	–	4.98 ± 3.66	F = 0.799	0.630	η^2 < 0.01
Age: 26–35	4.69 ± 3.75	2.02 ± 1.47			
Age: 36–45	12.01 ± 10.25	9.58 ± 14.73			
Age: 46–55	10.52 ± 4.47	7.18 ± 5.21			
Age: 56–65	7.42 ± 7.08	7.99 ± 9.52			
Age: ≥ 66	9.54 ± 7.56	8.37 ± 11.99			
Area: Rural	10.09 ± 7.41	6.21 ± 5.26	F = 1.330	0.260	η^2 = 0.01
Area: Urban	8.93 ± 7.21	8.68 ± 12.25			
Profession: Active	8.16 ± 6.61	8.60 ± 11.32	F = 0.780	0.500	η^2 = 0.01
Profession: Inactive	9.85 ± 7.57	7.78 ± 10.68			
Cancer: Malignant	11.82 ± 9.4	11.2 ± 15.73	F = 1.510	0.080	η^2 = 0.02
Cancer: Non-malignant	12.78 ± 14.2	7.01 ± 5.29			
Craniocerebral trauma	9.68 ± 7.89	8.05 ± 9.3			
Cerebral hemorrhage	7.76 ± 3.6	12.82 ± 13.71			
aSAH	7.32 ± 2.46	11.93 ± 20.73			
UIAs	–	3.37 ± 3.74			
Other diagnoses (avg)	4.84 ± 2.08	2.54 ± 1.51			
Nutrition: <3 points	8.92 ± 7.81	7.37 ± 9.78	F = 2.440	0.060	η^2 = 0.01
Nutrition: ≥3 points	9.40 ± 7.03	12.78 ± 16.36			
Group of infection factors: Group 0	12.76 ± 11.77	–	F = 1.230	0.290	η^2 = 0.02
Group of infection factors: Group I–IV (avg)	8.96 ± 8.00	8.35–10.16			
Season: Spring	10.28 ± 4.90	6.39 ± 4.99	F = 1.330	0.230	η^2 = 0.01
Season: Summer	6.87 ± 3.89	7.56 ± 10.70			
Season: Autumn	8.74 ± 7.61	10.12 ± 15.83			
Season: Winter	11.84 ± 11.95	8.11 ± 8.48			

Note: Comparisons of NLR (continuous) across subgroups were performed using ANOVA (F) unless stated otherwise. Effect sizes are reported as η^2. The p-values are reported as x.xxx; values <0.001 are shown as <0.001. "–" indicates that no patients were present in the respective subgroup. If a range is presented (eg, for aggregated Groups I–IV), it denotes the span of subgroup means in controls.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; HAIs, hospital-acquired infections; GCS, Glasgow Coma Scale; ASA, American Society of Anesthesiologists; aSAH, aneurysmal subarachnoid hemorrhage; UIAs, unruptured intracranial aneurysms.

scores of 8–3, the mean NLR in the HAIs group was 8.91 and in the control group 17.89, a difference that was also statistically significant (p = 0.0001) (Table 3).

A significant relationship was found for the mode of surgery - in elective surgeries the mean NLR in the HAIs group was 9.66, while in the control group it was 6.22; for urgent surgeries the mean NLR in the HAIs group was 9.38, while in the control group it was 9.64 (F = 3.65, p = 0.01) (Table 3).

For the ASA scale, the mean overall NLR for the HAIs group was M = 9.59 and for the control group M = 7.24, a difference that was statistically significant (F = 7.33, p = 0.01). The HAIs group had the highest NLR values across all ASA categories (Table 3). However, an exception was observed in the ASA 4 subgroup, where the control group demonstrated a higher mean NLR value than the HAIs group.

Deaths in the control group were associated with higher NLR values (M = 15.19) compared with survivors (M = 6.84). In the HAIs group, conversely, patients who died had a lower mean NLR (M = 7.9) than survivors (M = 9.58). These differences were statistically significant (p = 0.001) (Table 3). When comparing the NLR between the HAIs and control groups for deaths alone, the differences did not reach statistical significance (F = 3.32; p = 0.074). Similarly, in the case of survivors, the NLR value was also not statistically significant (F = 3.755; p = 0.054). In both cases, a potential statistical trend was observed, which may suggest some association that requires further analysis (Table 3).

The relationship between NLR and hospitalization duration was assessed using both Spearman's rank correlation and a generalized linear model (GLZ).The results of these analyses are summarized in Tables 5 and 6. Although the sample sizes were sufficiently large to permit the use of parametric tests under the central limit theorem, we employed non-parametric methods and a generalized linear model (GLZ) to better account for the skewed and bimodal distribution of hospitalization duration.

To further examine this relationship, both nonparametric and multivariate methods were applied. Due to the markedly skewed and bimodal distribution of hospitalization time (40 days in HAIs vs 5.4 in controls), we calculated Spearman's rank correlation: in the control group (n = 181): ρ = 0.089, p = 0.233; in the HAIs group (n = 93): ρ = 0.095, p = 0.413 (Table 5).

These correlations were weak and not statistically significant. To account for potential confounding and distribution shape, we used a GLZ with a log link and normal distribution. In this model: NLR was not a significant predictor of hospitalization time (β = –0.009, SE = 0.011, p = 0.404); group membership (HAIs vs control) was a strong independent predictor (β = 1.021, SE = 0.192, p < 0.001) (Table 6).

Table 5 Spearman's Rank Correlation Between NLR and Hospitalization Time

Group	N	Spearman's R	t(df)	p-value
Control	181	0.089	1.196	0.233
HAIs	93	0.095	0.823	0.413

Table 6 Generalized Linear Model (GLZ) Predicting Hospitalization Time (Log Link, Normal Distribution)

Predictor	Estimate (β)	SE	Wald χ^2	95% CI (Lower)	95% CI (Upper)	p-value
Intercept	2.772	0.209	176.64	2.363	3.181	<0.001
NLR	−0.009	0.011	0.70	−0.031	0.013	0.404
HAIs group	1.021	0.192	28.38	0.645	1.397	<0.001

Note: P-values are reported as p = x.xxx (or p < 0.001 when below the reporting threshold); values < 0.05 are bolded. Spearman correlation showed no significant monotonic association between NLR and hospitalization time in either group. In the GLZ model, NLR was not a significant predictor, while group status (HAIs vs control) was a strong and independent predictor of hospital stay duration. Non-significant results may reflect limited statistical power. Spearman's R is reported as an effect size for non-parametric correlation.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; SE, standard error; CI, confidence interval; HAIs, hospital-acquired infections.

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These results suggest that hospitalization time is primarily influenced by group status (presence of HAIs), and NLR has no independent predictive value in this context. The model residuals support this conclusion, showing a clear group-based clustering.

Survival and Prognostic Analysis of NLR

To comprehensively evaluate the prognostic relevance of NLR in neurosurgical patients, we conducted survival analyses, ROC-based threshold identification, and subgroup comparisons by cut-off value.

Kaplan–Meier Survival Curves

Kaplan–Meier survival curves demonstrated a decreasing probability of survival with increasing NLR values in both groups (Figure 2).

In the HAIs group, at low NLR values (below 9.5), the probability of survival was markedly elevated, around 80%. An abrupt decline in survival probability was observed for NLR > 17.7, where the cumulative probability of survival decreased from 65% to 40%. The Kaplan-Meier curve exhibited a stepwise pattern, with clearly marked points (Figure 2A).

In the control group, a cumulative survival probability of 80% occurred in patients with an NLR between 0 and 11.95. The curve exhibited a gradual slope, without clearly defined cutoff points (Figure 2B). In the control group, a broader distribution of NLR values was observed, reaching up to 100, indicating a more diverse population in this group. In the HAIs group, the probability of survival decreased more rapidly, already at an NLR of about 20 to about 50%. In the control group, the decline was less steep. At an NLR of 20, the probability of survival remained at about 60–70% (Figure 2A and B).

Survival Analysis with Cox Proportional Hazards Model

To statistically validate the survival differences observed in the Kaplan–Meier curves, we conducted additional analyses using the Log rank test and the Cox proportional hazards regression model (Table 7).

The Log rank test comparing survival between NLR strata (≥ 17.7 vs < 17.7) did not reveal a statistically significant difference ($p = 0.394$; Table 8). However, the statistical power of the test was limited (7.0% with $N = 120$ per group, $\alpha = 0.05$), indicating that the sample size may have been insufficient to detect subtle survival differences.

The Cox regression model, with NLR as a continuous variable and group (HAIs vs control) as a binary covariate, yielded the following results (Table 7):

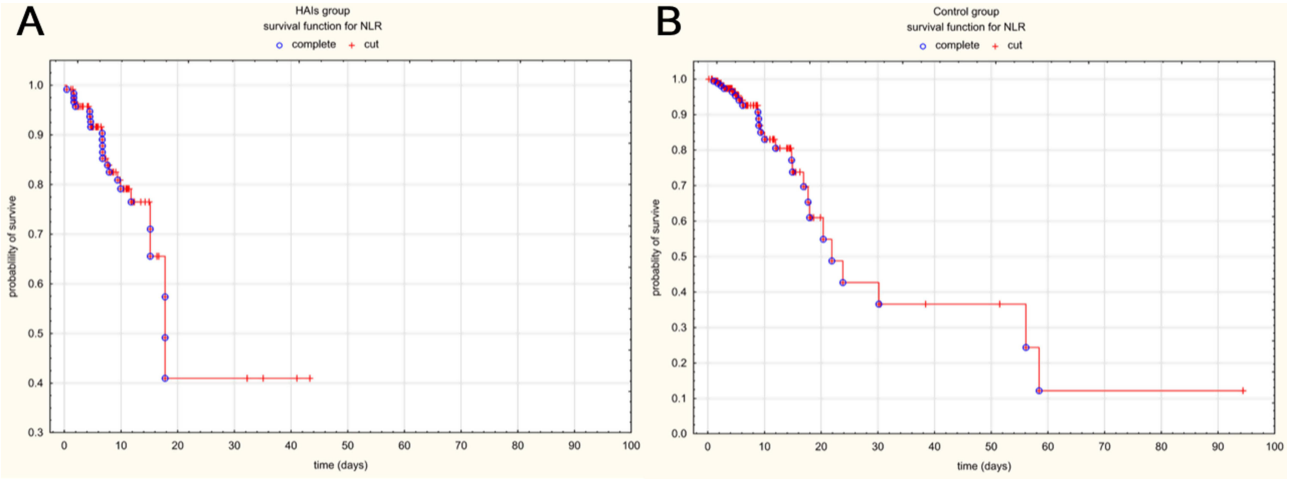

Figure 2 Kaplan–Meier survival curves showing the probability of death in the HAIs group (**A**) and the control group (**B**).
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; HAIs, hospital-acquired infection.

Table 7 Cox Proportional Hazards Regression Model for NLR and Group Assignment (HAIs Vs Control) as Predictors of Mortality

Variable	β (coefficient)	SE	HR (95% CI)	Wald χ^2	p-value
NLR	0.029	0.010	1.029 (1.009–1.051)	7.75	0.005
HAIs group[†]	–0.873	0.246	0.175 (0.067–0.457)	12.63	<0.001

Note: Cox proportional hazards regression model was used to evaluate the association between NLR and HAIs group with mortality as the outcome. Hazard ratios (HR) with 95% confidence intervals (CI) are reported as effect size estimates. The p-values are reported as p = x.xxx (or p < 0.001 when below the reporting threshold); values **<**0.05 are bolded. Both NLR and HAIs group were independently associated with mortality. Wald χ^2 statistics are provided for each predictor. [†]Reference: control group. **Abbreviations**: NLR, neutrophil-to-lymphocyte ratio; HR hazard ratio; CI, confidence interval; SE, standard error; HAIs, hospital-acquired infections.

Table 8 ROC and Survival-Based Evaluation of NLR Cutoff Value (17.7)

Analysis	Value
AUC (ROC curve for NLR predicting in-hospital mortality)	0.691
Optimal cutoff (Youden Index)	17.7
Sensitivity / Specificity (%)	57.1% / 89.4%
Kaplan–Meier Log rank test (NLR ≥ 17.7 vs < 17.7)	p = 0.394 (power = 7%)
Cox regression HR for NLR (continuous)	HR = 1.029 (95% CI: 1.009–1.051), p = **0.005**

Note: P-values are reported as p = x.xxx (or p < 0.001 when below the reporting threshold); values < 0.05 are bolded. Receiver Operating Characteristic (ROC) analysis was used to determine the optimal threshold of neutrophil-to-lymphocyte ratio (NLR) for predicting in-hospital mortality. The cutoff of 17.7 was identified using the Youden Index. Discriminative ability was assessed using the area under the curve (AUC). Sensitivity and specificity at this cutoff are reported. Prognostic value was further evaluated using Kaplan–Meier survival analysis (Log rank test) and Cox proportional hazards modeling. Kaplan–Meier survival analysis had limited statistical power (7%), and results should be interpreted cautiously. Subgroup ROC results (control vs HAI) are presented in the Results text and not included here to maintain table clarity. Hazard ratios with 95% CI are reported as effect size estimates. **Abbreviations**: NLR, neutrophil-to-lymphocyte ratio; ROC, receiver operating characteristic; AUC, area under the curve; HR, hazard ratio; CI, confidence interval.

- NLR was identified as an independent predictor of mortality, with a hazard ratio (HR) = 1.029 (95% CI: 1.009–1.051; p = 0.005), indicating that each unit increase in NLR was associated with a 2.9% higher risk of death.
- HAIs group membership was also significantly associated with a lower hazard of death (HR = 0.175; 95% CI: 0.067–0.457; p < 0.001; reference = control). These results indicate that NLR functions as an independent prognostic biomarker for mortality, regardless of infection status.

These findings provide statistical support for the prognostic relevance of NLR and complement the descriptive Kaplan–Meier survival curves presented in Figure 2. The absence of statistical significance in the Log rank test is most likely related to the limited sample size and low-test power. Future studies involving larger and more diverse cohorts are recommended to confirm these results and further explore NLR-based risk stratification.

In both groups, very high NLR values (eg, >40) were associated with a very low probability of survival (approximately 30% or less). However, the decline was more gradual in the control group, whereas it was more abrupt in the HAIs group (Figure 2A and B).

Prognostic Value of NLR Cut-off ≥17.7 – ROC Analysis

To further assess the prognostic utility of the neutrophil-to-lymphocyte ratio (NLR), we conducted a receiver operating characteristic (ROC) analysis to identify a threshold value associated with in-hospital mortality. The ROC curve for the entire cohort yielded an area under the curve (AUC) of 0.691 (95% CI: 0.587–0.790; p = 0.001), indicating fair discrimination (Table 8). The optimal cut-off value based on the Youden index was 17.7, with a sensitivity of 57.1%

and a specificity of 89.4%. This threshold corresponds to the point at which a balance between true positive and false positive rates was maximized in our sample.

The same analysis conducted within the control group showed an even higher discriminatory ability of NLR for predicting mortality (AUC = 0.728; 95% CI: 0.592–0.864; p = 0.001), with sensitivity and specificity of 47.6% and 89.2%, respectively. In contrast, ROC analysis in the HAIs group did not reach statistical significance (AUC = 0.519; 95% CI: 0.307–0.731; p = 0.840), suggesting that NLR may have limited predictive value in this subgroup, possibly due to immunosuppression or other confounding clinical factors. Subgroup-specific ROC results are reported here in the text, whereas Table 8 summarizes the overall ROC and the survival-based evaluation at the NLR cut-off. While the discriminatory power of NLR was limited in patients with HAIs, its predictive value in uninfected patients warrants further investigation as part of a risk stratification strategy.

These results support the use of NLR ≥ 17.7 as a clinically meaningful prognostic threshold, particularly in non-infected neurosurgical patients. The findings are in line with prior literature, which has reported heterogeneous NLR cut-off values depending on clinical context and outcome measure. However, the moderate sensitivity and lack of external validation highlight the need for cautious interpretation and further multicenter studies to confirm this threshold.

Clinical Impact of the 17.7 Cut-off

In the overall population, NLR ≥ 17.7 was significantly associated with increased in-hospital mortality (40% vs 12.61% for NLR < 17.7). Pearson's chi-square test (χ^2 = 11.025; p = 0.00090), Yates' correction (p = 0.00277), and Fisher's exact test (p = 0.00359) all confirmed statistical significance. Effect size measures including the φ coefficient (0.207) and tetrachoric correlation (0.437) indicated a moderate association. Spearman's rank correlation (R = 0.207; p = 0.00084) supported this finding (Table 9).

In the HAIs subgroup, no significant association was observed between NLR categories and mortality (20.0% vs 16.67%). Chi-square, Yates, and Fisher tests all yielded non-significant results (p > 0.46). Effect sizes (φ = 0.022;

Table 9 Association Between NLR Categories and Mortality in HAIs and Control Groups

Death / NLR Category	**Total Group**		**HAIs Group**		**Control Group**	
	NLR<17.7	**NLR ≥ 17.7**	**NLR<17.7**	**NLR ≥ 17.7**	**NLR<17.7**	**NLR ≥ 17.7**
Deaths*, n (%)	30 (12.61)	8 (40.00)	12 (16.67)	1 (20.00)	18 (10.84)	7 (46.67)
Survived, n (%)	208 (87.39)	12 (60.00)	60 (83.33)	4 (80.00)	148 (89.16)	8 (53.33)
χ^2 test statistic:	**Test Value (P value)**		**Test Value (P value)**		**Test Value (P value)**	
Pearson χ^2	11.025 (**0.001**)		0.037 (0.847)		14.830 (**0.000**)	
Unweighted χ^2 (NW)	8.441 (**0.004**)		0, 035 (0.851)		10.678 (**0.001**)	
Yates' χ^2	8.951(**0.003**)		0.181 (0.467)		11.974 (**0.001**)	
Fisher's exact test (one-sided)	**(0.004)**		(0.614)		**(0.001)**	
Fisher's exact test (two-sided)	**(0.004)**		(1.000)		**(0.001)**	
φ for 2×2 tables	0.207		0.022		0.286	
Tetrachoric correlation	0.436		0.275		0.554	
Contingency factor	0.202		0.061		0.275	
Somers (X|Y)	0.156		0.014		0.358	
Somers (Y|X)	0.274		0.033		0.229	
Spearman's rank correlation (ρ)	0.207; t=3.380 (p=**0.001**)		0.022; t=0.190 (p=0.850)		0.286; t=3.997 **(p=0.001)**	

Note: Bolded p-values indicate statistical significance (p < 0.05). Patients were categorized based on the neutrophil-to-lymphocyte ratio (NLR) into two groups: NLR < 17.7 and NLR ≥ 17.7. Associations with in-hospital mortality were evaluated using Pearson's χ^2-test, Yates-corrected χ^2, unweighted χ^2 (NW), Fisher's exact test (one- and two-sided), and non-parametric correlation analyses. Effect sizes were expressed using φ (phi coefficient), which quantifies the strength of association in 2×2 tables, as well as tetrachoric correlation, contingency coefficient, Somers' D (X|Y and Y|X), and Spearman's rank correlation (ρ). *p* values for Spearman correlation and other tests were provided. * Denotes in-hospital mortality.
Abbreviations: NLR, neutrophil-to-lymphocyte ratio; HAIs, hospital-acquired infections; χ^2, chi-square test statistic; φ, phi coefficient; ρ, Spearman rank correlation; n, number; %, percentage within group.

Table 10 Comparison of Rank Sums Between NLR < 17.7 and NLR ≥ 17.7 in the Total Population, HAIs Group, and Control Group

Group	Rank Sum (NLR < 17.7)	Rank Sum (NLR ≥ 17.7)	Test Statistic (Z)	p-value	N (NLR < 17.7)	N (NLR ≥ 17.7)	Exact p-value
Total	30,740.5	2,670.5	−0.250	0.803	238	20	0.803
HAIs	2,823.0	180.0	0.230	0.764	72	5	0.771
Control	14,947.5	1,523.5	−0.813	0.416	166	15	0.418

Note: P-values are reported as p = x.xxx (or p < 0.001 when below the reporting threshold); values < 0.05 are bolded. Mann–Whitney *U*-tests compared hospitalization times between NLR < 17.7 and NLR ≥ 17.7 within the total cohort, HAIs, and controls. The "Exact p-value" column reports exact distribution-based p-values (two-sided). Small sample sizes in the NLR ≥ 17.7 subgroup (N = 20, 5, and 15, respectively) limit statistical power and precision of estimates.

Abbreviations: NLR, neutrophil-to-lymphocyte ratio; HAIs, hospital-acquired infections; Z, standardized test statistic.

tetrachoric correlation = 0.275) suggested a weak association, and Spearman's R = 0.022 (p = 0.84987) confirmed the absence of a significant relationship (Table 9).

In contrast, the control group showed a strong association between elevated NLR and mortality (46.67% vs 10.84%). Pearson's chi-square (χ^2 = 14.830; p = 0.00012), Yates (p = 0.00054), and Fisher (p = 0.00128) were all highly significant. The φ coefficient (0.286) and tetrachoric correlation (0.554) indicated a moderate to strong effect size. Spearman's R = 0.286 (p = 0.0007) corroborated these findings (Table 9). These results reinforce the prognostic relevance of NLR ≥ 17.7, particularly in uninfected neurosurgical patients.

Differences in hospitalization duration between patients with NLR < 17.7 and NLR ≥ 17.7 did not reach statistical significance in any of the analyzed subgroups (Table 10). In the total population, the Mann–Whitney *U*-test yielded Z = –0.25, p = 0.803. In the HAIs group, Z = 0.23, p = 0.764; in the control group, Z = –0.81, p = 0.416. These results indicate that NLR stratification based on the 17.7 threshold was not associated with differences in length of hospital stay.

Discussion

Epidemiology and Clinical Context

In this neurosurgical cohort, the incidence of HAIs was approximately 3%, which - although relatively low - remains within the range reported in neurosurgical units (2.9%–10%), depending on institutional characteristics, patient complexity, and procedural profile.[18,32] Patients with HAIs demonstrated a more severe clinical course, a higher prevalence of major neurological diagnoses, and markedly prolonged hospitalization compared with non-infected controls. The data reinforce the established association between acute neurosurgical illness, invasive procedures, and increased susceptibility to HAIs.[18,33] Notably, patients undergoing urgent surgical interventions had a disproportionately higher infection rate, highlighting perioperative exposure and immune compromise as key contributors.[34]

In-hospital mortality in the nosocomial infection group reached 16%, which is comparable to the results of previous neurosurgical cohorts.[35] This likely reflects the combined burden of infection and complex comorbidity profiles typical of this population, highlighting the importance of multidimensional risk assessment. Incorporating physiological indices, such as the ASA physical status classification, into routine surveillance and prophylaxis strategies may enhance risk stratification.[31,36] Although comorbidities were not systematically recorded in this study, the observed mortality rate suggests their probable contribution to adverse outcomes, consistent with prior literature.

Interestingly, in-hospital mortality rates were comparable between the HAIs and control groups, despite the markedly worse baseline clinical condition in the HAIs cohort. This finding likely reflects the study's design, in which controls were matched for age, gender, and mortality status to allow a focused comparison of inflammatory markers rather than raw survival outcomes.[18] While such matching reduces confounding, it also narrows between-group differences in mortality, potentially masking the true impact of HAIs on survival observed in unadjusted analyses in other studies.[37] Moreover, the relatively small absolute number of deaths in both groups may have limited the statistical power to detect minor differences.

NLR as an Accessible Biomarker in Neurosurgical Populations

Beyond epidemiology, this study evaluated the NLR as an easily obtainable marker of systemic inflammation in the context of HAIs. NLR was significantly higher in infected patients compared with controls, supporting its role as a surrogate inflammatory marker, in agreement with previous neurosurgical and critical care reports.[1,3] No significant differences were observed by sex or age group, in line with evidence suggesting minimal demographic influence.[38] Interestingly, in our cohort, peak NLR values in the HAIs group were observed in patients aged 36–45 years, whereas in controls the highest values occurred in those aged >65 years.

When stratified by diagnosis, the highest NLR values in the HAIs group were seen in patients with CNS tumors, consistent with evidence linking elevated NLR to tumor burden, metastatic potential, and poorer survival in oncological settings.[39,40] In the control group, peak NLR values occurred in acute cerebrovascular events, including intracerebral hemorrhage and aneurysmal subarachnoid hemorrhage, consistent with literature supporting its prognostic value for complications such as rebleeding and delayed cerebral ischemia.[9,41,42]

Interestingly, NLR did not independently predict length of stay in either group. While sensitive to acute inflammatory activation, its prognostic capacity for long-term outcomes such as hospitalization duration appears limited.[3,43] Conversely, the mere presence of HAIs proved to be a strong, independent predictor of length of stay (LOS), with a median difference of 40 days compared to 5.4 days in the control group, underscoring the substantial clinical burden and prolonged recovery associated with HAIs.[44–46]

Comparison with Prior Studies

Our observations accord with recent neurosurgical reports linking inflammatory indices to postoperative infectious complications. Chen et al developed a prediction model for postoperative pulmonary infection after aneurysmal subarachnoid hemorrhage based on inflammatory markers, highlighting the prognostic utility of systemic inflammation metrics.[26] Pahwa et al reported predictors of neurosurgical postoperative infections in a retrospective analysis.[27] Our study extends this evidence by evaluating NLR in a general neurosurgical cohort, examining hospital-acquired infection and in-hospital mortality as outcomes, and deriving a data-driven NLR threshold.

Neurological State and the "Survivor Paradox"

An apparently paradoxical finding was the higher NLR values in HAIs survivors compared with non-survivors. This is biologically and methodologically plausible. During the early pro-inflammatory phase of severe infection, elevated NLR reflects strong innate immune activation; however, in later stages, sepsis-induced immunosuppression—characterized by lymphocyte apoptosis and impaired myelopoiesis—may result in declining NLR preceding death.[5,47,48]

In neurosurgical patients, CNS injury-induced immunosuppression, mediated through activation of the sympathetic-adrenal and hypothalamic-pituitary-adrenal axes, further suppresses adaptive immunity and alters inflammatory kinetics.[21] Glucocorticoid therapy, widely used for cerebral edema, can independently elevate NLR via neutrophil demargination and lymphocyte redistribution.[49]

Methodological factors, such as timing bias—where patients with fatal neurological deterioration may die before mounting a full inflammatory response—and the limited number of deaths in the HAIs subgroup, may also contribute. These considerations reinforce the need to interpret peri-terminal NLR values in light of disease stage, CNS injury-related immune alterations, and treatment-related confounders.

Prognostic Threshold of NLR ≥17.7

An NLR threshold of 17.7 in our cohort yielded a sensitivity of 57.1% and specificity of 89.4% for predicting in-hospital mortality, placing it at the upper end of values reported in high-acuity populations. In septic patients, Wen et al[50] identified optimal cut-offs of 10.77 (day 1), 17.54 (day 2), and 14.40 (day 3), with higher values strongly linked to mortality. Our admission-based threshold's similarity to the day 2 value reported by Wen et al may reflect early onset of severe inflammation in our cohort.

Neurocritical care literature shows less consensus on numeric cut-offs. A systematic review and meta-analysis by Guo et al[41] found that NLR > 7.5 was consistently associated with mortality and poor functional outcomes in spontaneous intracerebral

hemorrhage, although thresholds varied across studies. In traumatic brain injury, Sabouri et al[51] and Ghozy et al[40] concluded that elevated NLR is repeatedly associated with adverse outcomes, but no universal cut-off can be established due to heterogeneity in populations, timing, and outcome definitions.

Most neurocritical and neurotrauma studies report admission thresholds well below our value, typically 7–10,[41,52,53] highlighting the extreme inflammatory burden observed in our patients. Notably, in our cohort, NLR ≥17.7 strongly predicted mortality in uninfected patients but had no significant predictive value in those with HAIs, possibly reflecting immune dysregulation or confounding clinical factors in infected individuals. This underscores the need for context-specific validation of NLR thresholds before broad clinical adoption.

NLR Compared to CRP, PCT, and SOFA

C-reactive protein (CRP), procalcitonin (PCT), and clinical scores such as the Sequential Organ Failure Assessment (SOFA) are established tools for infection assessment,[54] but each has limitations. NLR's key advantage lies in its rapid responsiveness—changes can occur within approximately six hours of physiological stress, faster than CRP or total white blood cell count.[55] This makes NLR particularly useful for repeated monitoring and early risk stratification in high-risk neurosurgical settings.

Studies across surgical populations indicate that combining NLR with other biomarkers, such as PCT or CRP, may improve diagnostic accuracy and enable earlier intervention.[56] Peng et al[57] reported moderate diagnostic accuracy of NLR (AUC = 0.80) for postoperative infection in orthopedic surgery, suggesting greatest utility in multimodal approaches. The diagnostic yield of any biomarker is influenced by surgical type, postoperative timing, and patient-specific factors, supporting individualized, multi-biomarker strategies to optimize infection surveillance and guide timely interventions.[55]

Study Limitations

This study has several limitations: (1) its single-center, retrospective design limits generalizability and precludes establishing causal relationships; (2) comorbidities were not systematically recorded, preventing adjustment for their potential confounding effects; (3) NLR was measured only at admission — serial measurements could reveal prognostically relevant dynamic trends; (4) perioperative use of steroids, antibiotics, and other immunomodulatory agents was not fully controlled and may have influenced NLR values; (5) the relatively low incidence of HAIs compared with some reports may reflect institutional practices, patient case-mix, definitional differences, and/or potential underreporting related to incomplete documentation or absence of microbiological confirmation in some cases; (6) information on the exact ward location during hospitalization (eg, high-dependency vs general ward) was not available in the retrospective dataset, which could have provided additional insights into patient severity and intensity of care; and (7) several HAIs subtypes had small cell counts and culture data were incomplete, limiting power for subtype- or pathogen-specific analyses and potentially introducing residual confounding; therefore, subtype- or pathogen-adjusted models were not fitted. Because standardized comorbidity fields and procedure duration were incompletely recorded, residual confounding cannot be excluded; accordingly, we report effect sizes alongside p-values and recommend cautious interpretation.

Clinical Implications and Future Directions

Our findings suggest that prolonged hospitalization in neurosurgical patients is primarily driven by HAIs, while NLR - although a valuable inflammatory severity marker - does not independently predict LOS. Despite this, NLR remains a pragmatic prognostic marker because it is inexpensive and universally available from routine admission blood counts, and can complement (rather than replace) CRP/PCT in early risk stratification, particularly where access to more specific biomarkers is limited. The high cut-off identified here reflects extreme systemic inflammation in the sickest patients but also underscores the lack of a universal threshold in neurocritical care.

Future research should aim to validate context-specific NLR thresholds, integrate NLR into multimodal prognostic models with CRP, PCT, and SOFA, and evaluate its role in early detection of infection-related complications. Prospective, multicenter studies with standardized sampling and comprehensive comorbidity assessment will be essential to refine its prognostic utility and support clinical implementation.

Conclusion

In this neurosurgical cohort, the NLR was significantly associated with in-hospital mortality in patients without HAIs, with a cut-off of ≥17.7 demonstrating fair discriminatory ability. In patients with HAIs, its prognostic value was limited, likely due to immune dysregulation or clinical confounders, and NLR did not correlate with hospitalization time in any group. While NLR is a cost-effective and rapidly obtainable marker of systemic inflammation, its prognostic performance appears context-specific and not superior to established tools. Key limitations of this study include its single-center retrospective design, lack of serial NLR measurements, and potential confounding by unmeasured variables such as corticosteroid or antibiotic use. Incorporating NLR into multimodal risk assessment frameworks - including CRP, procalcitonin, and composite clinical scores - may enhance early detection and targeted management of high-risk patients.

Take-Home Message

NLR may serve as a readily available prognostic marker in selected neurosurgical populations, but its clinical utility requires confirmation in larger, multicenter prospective studies.

Data Sharing Statement

De-identified data underlying this article are available from the corresponding author upon reasonable request. Data will be shared without undue reservation for research purposes consistent with ethical approval and patient confidentiality.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki (2013 revision). Approval was obtained from the Bioethics Committee of Nicolaus Copernicus University in Toruń, Collegium Medicum in Bydgoszcz (approval No. 182/2022). Owing to the retrospective design and use of de-identified data, the requirement for informed consent was waived by the Committee. All patient data were anonymized prior to analysis and handled with strict confidentiality. The study was reported in accordance with the RECORD guideline.

Author Contributions

Renata Jabłońska: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Validation, Visualization, Writing - Original Draft, Writing - Review & Editing. Robert Ślusarz: Funding acquisition, Supervision, Methodology, Writing - Review & Editing Magdalena Zając: Formal analysis, Validation, Visualization, Writing - Review & Editing. Agnieszka Królikowska: Data curation, Investigation, Writing - Review & Editing. Karolina Filipska-Blejder: Data curation, Investigation, Writing - Review & Editing. Paweł Sokal: Conceptualization, Methodology, Writing - Review & Editing.

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