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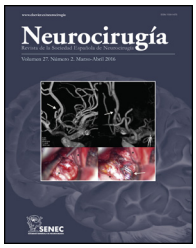

Clinical Research

Relationship between NLR (Neutrophil/Lymphocyte ratio) value and clinical outcome in patients with external ventricular drainage due to intraventricular hemorrhage

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ARTICLE INFO

Article history:
Received 28 June 2024
Accepted 17 October 2024

Keywords:
Neutrophil/Lymphocyte ratio
Intraventricular hemorrhage
Outcome

ABSTRACT

Background: Intraventricular hemorrhages (IVH) are common pathologies in neurosurgery practice and are associated with the worst clinical outcome among all intracranial hemorrhages. Blood in the ventricles is thought to worsen the clinical condition by triggering inflammatory processes. In recent years, NLR value is a frequently used inflammatory parameter, and there are many publications reporting that a high NLR value is an important marker in predicting the severity of inflammation.

Our study aimed to evaluate the effect of NLR values at admission on the clinical outcome of patients undergoing EVD due to IVH in our clinic.

Material and methods: In our study, age and gender data, admission Glasgow Coma Scale (GCS), NLR value at the time of admission and clinical status at discharge of 36 patients, who underwent EVD following IVH in our hospital neurosurgery clinic between 2019 and 2024, were examined.

Results: Of the 36 cases in our study, 16 were female and 20 were male. For all cases, the mean age was 61.88, and the mean GCS values at admission were calculated as 8.5. In the laboratory of our hospital, the normal NLR range was determined as 0.78-3.53, and the mean NLR values at admission were evaluated as 16.57. When the clinical outcomes of the cases were examined, it was seen that 30 cases ended with exitus after intensive care follow-up, and 6 cases were discharged with good clinical outcomes (GCS:15). The mean NLR value was calculated as 18.00 for the patients who ended with exitus and 8.12 for the patients discharged with good clinical outcomes.

DOI of original article: https://doi.org/10.1016/j.neucir.2024.10.007.

Abbreviations: NLR, Neutrophil/Lymphocyte Ratio; EVD, external ventricular drainage; IVH, intraventricular hemorrhage; GCS, Glasgow Coma Scale; CRP, C-reaktive protein; WBC, white blood count; HT, hypertension; DM, diabetes mellitus; CAD, coroner artery disease; HF, heart failure; AF, atrial fibrillation; RA, romatoid artritis; CKD, chronic kidney disease; DMD, Duchenne muscular dystrophy; MS, multiple sclerosis.

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https://doi.org/10.1016/j.neucie.2024.11.005

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Conclusion: NLR, which has been used to determine the severity of inflammation in recent years, has been reported to be a marker that can predict clinical outcomes of many diseases. In our study, NLR was observed to be high at admission in all cases, but it was significantly higher in the cases ending with exitus than in the cases not ending with exitus. As a result, it is thought that NLR value is a parameter that can be used to predict the clinical course in IVH patients undergoing EVD.

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Relación entre el valor NLR (relación neutrófilos/linfocitos) y el resultado clínico en pacientes con drenaje ventricular externo debido a hemorragia intraventricular

Palabras clave:
Relación neutrófilos/linfocitos
Hemorragia intraventricular
Resultado

RESUMEN

Antecedentes: Las hemorragias intraventriculares (Hiv) son patologías comunes en la práctica de la neurocirugía y se asocian con el peor resultado clínico entre todas las hemorragias intracraneales. Se cree que la sangre en los ventrículos empeora la condición clínica al desencadenar procesos inflamatorios. En los últimos años, el valor NLR es un parámetro inflamatorio utilizado con frecuencia y hay muchas publicaciones que informan que un valor NLR alto es un marcador importante para predecir la gravedad de la inflamación.
Nuestro estudio tuvo como objetivo evaluar el efecto de los valores de NLR al ingreso sobre el resultado clínico de los pacientes sometidos a EVE debido a Hiv en nuestra clínica.
Material y métodos: En nuestro estudio se utilizaron datos de edad y sexo, escala de coma de Glasgow (GCS) al ingreso, valor de NLR en el momento del ingreso y estado clínico al alta de 36 pacientes, a los que se les realizó EVE tras Hiv en la clínica de neurocirugía de nuestro hospital entre 2019 y 2024, fueron examinados.
Resultados: De los 36 casos de nuestro estudio, 16 fueron mujeres y 20 hombres. Para todos los casos, la edad media fue de 61,88 años y los valores medios de GCS al ingreso se calcularon como 8,5. En el laboratorio de nuestro hospital, el rango normal de NLR se determinó entre 0,78-3,53 y los valores medios de NLR al ingreso se evaluaron como 16,57. Cuando se examinaron los resultados clínicos de los casos, se observó que 30 casos terminaron con exitus después del seguimiento en cuidados intensivos y 6 casos fueron dados de alta con buenos resultados clínicos (GCS:15). El valor medio del INL se calculó como 18,00 para los pacientes que terminaron con exitus y 8,12 para los pacientes dados de alta con buena evolución clínica.
Conclusión: Se ha informado que el NLR, que se ha utilizado para determinar la gravedad de la inflamación en los últimos años, es un marcador que puede predecir los resultados clínicos de muchas enfermedades. En nuestro estudio, se observó que el INL al ingreso era elevado en todos los casos, pero fue significativamente mayor en los casos que terminaron en exitus que en los casos que no terminaron en exitus. Como resultado, se cree que el valor NLR es un parámetro que puede usarse para predecir el curso clínico en pacientes con Hiv sometidos a EVE.

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Introduction

Intraventricular hemorrhages (IVH) are common pathologies in neurosurgery practice and are associated with the worst clinical outcome among all intracranial hemorrhages. IVHs often occur in association with intraparenchymal hematomas or subarachnoid hemorrhage (SAH); however, IVH can rarely be observed in isolation.[1] In the majority of cases, bleeding occurs in the lateral ventricles, but it can also affect all ventricles or the third or fourth ventricles in isolation.[2] IVHs are a group of diseases with a very poor clinical course. Its 30-day mortality rate ranges between 30% and 52% in different series.[3,4] In the majority of cases, increased intracranial pressure and acute hydrocephalus caused by IVH are treated though the placement of external ventricular drainage (EVD).[5]

Complete blood count is a rapid and inexpensive laboratory test performed at hospital admission in patients diagnosed

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Table 1 – Distribution of demographic and clinical findings of patients.

Characteristics (N = 36)	n (%)	Mean ± SD	Median (min–max)
Gender			
Male	20 (55.6)		
Female	16 (44.4)		
Age		62 ± 17	62 (23–95)
Comorbidity	28 (77.8)		
HT	17 (60.7)		
DM	6 (21.4)		
CAD	11 (39.3)		
HF	2 (7.1)		
Stroke	3 (10.7)		
AF	5 (17.9)		
RA	1 (3.6)		
CKD	2 (7.1)		
Cancer	2 (7.1)		
DMD	1 (3.6)		
MS	1 (3.6)		
GCS on admission		8.5 ± 4.3	7.5 (3–15)
NLR		16.4 ± 8.9	14 (5.7–38.4)
CRP		27.3 ± 53.4	10.8 (0.2–294.3)
WBC		13.2 ± 5.4	12.8 (4.8–25.1)
Cause of bleeding			
Spontaneous/ Unidentified	21 (58.3)		
Aneurysm	11 (30.6)		
Trauma	2 (5.6)		
Infarct hemorrhage	1 (2.8)		
Post-op bleeding	1 (2.8)		
Graeb index		7.7 ± 3.1	8 (2–12)
Parenchymal hemorrhage	23 (63.9)		
Outcome			
Alive	6 (16.7)		
Dead	30 (83.3)		

with IVH. It can often provide information about its etiology. Values such as leukocyte, neutrophil, lymphocyte, platelet and monocyte are evaluated in the complete blood count examination and are frequently used as inflammation markers in many diseases.[6] Neutrophil/lymphocyte ratio (NLR) value obtained from complete blood count results has been frequently mentioned as an inflammatory marker in many publications in recent years. There are many publications recommending the use of NLR as an important marker indicating the severity of endothelial dysfunction and inflammation in the acute period in different clinical situations.[7,8] These publications report that high NLR is a marker of poor prognosis for cardiovascular diseases, infections, inflammatory pathologies and many types of cancer. Presence of blood in the intracranial region is thought to trigger inflammatory processes.[9] In recent years, publications mentioning the prognostic value of inflammatory markers and their effect on clinical outcome have been increasing after trauma and intracranial pathologies.[7,8]

Our study aimed to evaluate the effect of NLR values on the prognosis and clinical outcome of the cases at admission who underwent EVD due to increased intracranial pressure and/or hydrocephalus after IVH in our clinic.

Material and methods

For the study, necessary permissions were obtained from our Hospital Training Planning Board (TPB) dated 26.03.2024. (Number: E-62977267-771-240825582).

The study included 36 cases who underwent EVD after IVH in our hospital neurosurgery clinic between 2019 and 2024. All EVD patients with isolated ventricular hemorrhage, parenchymal hemorrhage accompanying IVH or subarachnoidal hemorrhage were included in the study. Additional chronic diseases, antiaggregant/anticoagulant use were not considered as exclusion criteria.

The cases' age, sex, comorbidities, Glasgow Coma Scale (GCS) scores at admission, NLR, CRP levels, white blood cell (WBC) count, cause of bleeding, Graeb index, accompanying parenchymal hemorrhage and clinical conditions at discharge were retrospectively evaluated using the hospital automation system. Patients were divided into two groups (Group-1 patients who survival and Group-2 patients were dead). All statistical analyses were performed on all above-mentioned criteria between two groups.

Results

The distribution of the patients' demographic and clinical findings are shown in Table 1. Among the patients, 55.6% (n = 20) of the patients were male and 44.4% (n = 16) were female. Age distrubution of the patients ranged from 23 to 95 years, and the mean patient age was 62 ± 17 years. The rate of comorbidities were 77.8% (n = 28) and the most common disease was hypertension. GCS of the patients on admission was ranged from 3 to 15 points (mean GCS = 8.5 ± 4.3). NL ratio of the patients on admission was ranged from 5.7-38.4 (mean

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Table 2 – Distribution of demographic and clinical findings.

Characteristics (N = 36)	Alive (n = 6)			Dead (n = 30)			p-Value
	n (%)	Mean ± SD	Median (min–max)	n (%)	Mean ± SD	Median (min–max)	
Gender							1.000
Male	3 (50)			17 (56.7)			
Female	3 (50)			13 (43.3)			
Age (y)		58 ± 16	49 (47–80)		63 ± 17	63 (23–95)	0.574
Comorbidity	4 (66.7)			24 (80)			0.596
GCS on admission		**13.8 ± 0.8**	**14 (13–15)**		**7.4 ± 3.9**	**6 (3–15)**	**0.001**
NLR		**8.1 ± 1.8**	**8.3 (5.7–10.3)**		**18 ± 8.9**	**15.5 (6.6–38.4)**	**0.002**
CRP		**5.2 ± 6.6**	**3.1 (0.4–17.4)**		**31.7 ± 57.5**	**12.9 (0.2–294.3)**	**0.023**
WBC		12 ± 6.2	9.1 (7.3–23.5)		13.5 ± 5.3	12.9 (4.8–25.1)	0.532
Cause of bleeding							0.777
Spontaneous/Unidentified	3 (50)			18 (60)			
Aneurysm	3 (50)			8 (26.7)			
Trauma	0 (0)			2 (6.7)			
Infarct hemorrhage	0 (0)			1 (3.3)			
Post-op bleeding	0 (0)			1 (3.3)			
Graeb index		**5.3 ± 2.7**	**5 (3–10)**		**8.2 ± 3**	**8.5 (2–12)**	**0.037**
Parenchymal hemorrhage	4 (66.7)			19 (63.3)			1.000

NLR = 16.4 ± 8.9). The most common etiology of bleeding was spontaneous/unidentified with 58.3% (n = 21), and the rate of accompanying parenchymal bleeding was 63.9% (n = 23). Graeb index of the patients on admission was between 2 and 12 points (mean Graeb index = 7.7 ± 3.1). For the outcome, 16.7% (n = 6) of the patients survived and 83.3% (n = 30) of the patients died.

Demographic and clinical findings of patients in Group-1and Group-2 are described in Table 2. In Group-1 (n = 6) GCS on admission was between 13-15 (mean = 13.8 ± 0.8), in Group-2 (n = 30) GCS on admission was between 3–15 (mean = 7.4 ± 3.9). For Group-1 (n = 6) NLR was between 5.7–10.3 (mean = 8.1 ± 1.8), in Group-2 (n = 30) NLR was between 6.6-38.4 (mean = 18 ± 8.9). In Group-1 (n = 6) Graeb index was between 3–10 (mean = 5.3 ± 2.7), in Group-2 (n = 30) Graeb index was between 2–12 (mean = 8.2 ± 3). There were statistically significant difference between the groups in the GCS, NLR and GRAEB index ($p < 0.05$). GCS measurements on admission was higher in survivors, while NLR and Graeb index scores were higher in patients who died. (Fig. 1)

The ROC curve results made to examine the differential effect of patients' survival in terms of Neutrophil/Lymphocyte (NLR) ratio, initial GCS values and Graeb index score are shown in Table 3, Fig. 2.

While the area under the curve for NLR was found to be 88.3%, the limit value was determined to be >10.5. The area under the curve shows the statistical significance of the discrimination ability of the diagnostic test. The area under the curve and limit values for other measurements are as follows; For CRP, the area under the curve was found to be 79.4% and the limit value was >7.5. For the Graeb index, the area under the curve was found to be 77.2% and the limit value was >6. Since the diagnostic test evaluated in our study was survival, it was determined that the value found for NLR had good discrimination ability (80%–90%), and the values found for CRP and GRAEB index had moderate discrimination ability (70%–80%).

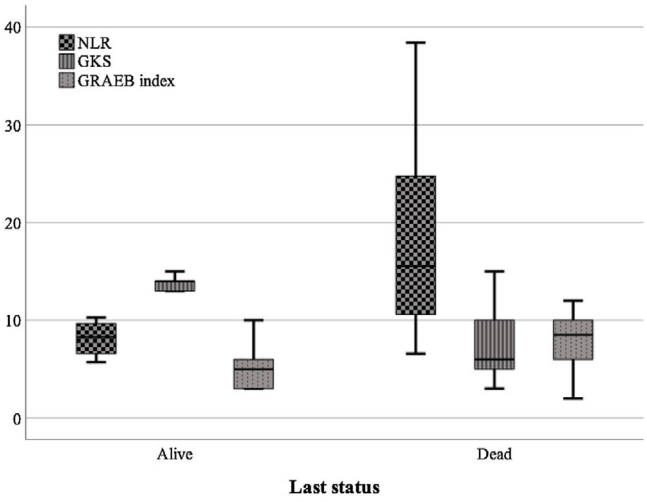

Fig. 1 – Box Plot of clinical measurements according to patients'.

Statistical analysis

Data analyses was performed using SPSS (Statistical Package for Social Sciences) Version 29.0 software (IBM SPSS Inc., Armonk, NY, USA) and MedCalc statistical software version 12.7.0.0 (MedCalc Software, Ostend, Belgium). A two-tailed Kolmogorov–Smirnov test was applied to examine for whether the continuous quantitative variables follow a Gaussian distribution. Characteristics of patients, as n (percent) or mean ± standard deviation (SD) and median (minimum–maximum) for categorical and continuous variables, respectively, and were compared among groups using chi-square or Mann–Whitney tests, as appropriate. ROC analysis was performed for the parameters that were thought to have a discriminative effect for survival and ROC curve was drawn. The p value was set at <0.05 for statistical significance.

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Table 3 – ROC analysis result for NLR measure of mortality.

Risk factor	AUC (95% CI)	Cut-off	p-Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
NLR	0.883 (0.771–0.996)	>10.50	0.003	76.7	100.0	100.0	46.2
GCS	0.894 (0.793–0.996)	≤12.00	0.024	83.3	100.0	100.0	54.5
Graeb index	0.772 (0.574–0.970)	>6.00	0.038	66.7	83.3	95.2	33.3

PPV: positive predictive value; NPV: negative predictive value.

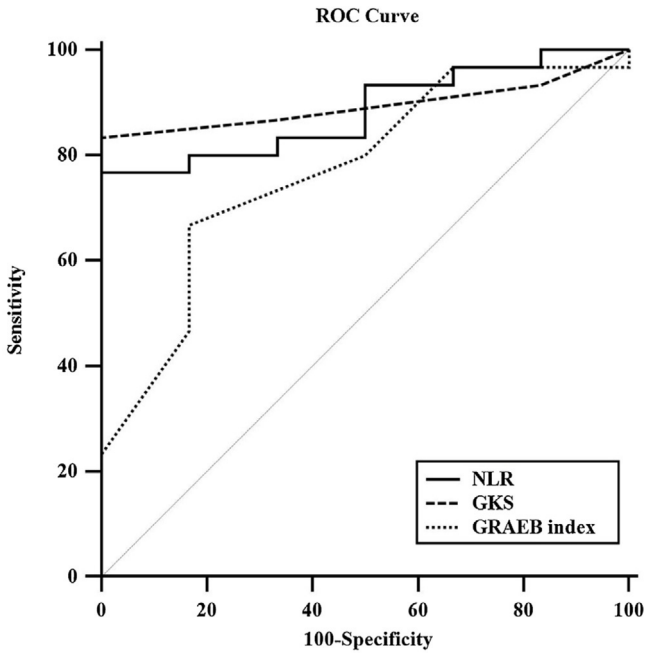

Fig. 2 – ROC curve for NLR measurement of mortality.

Discussion

Without considering the presence of intraventricular component, intracranial hemorrhage and subarachnoid hemorrhages constitute 10–15% of all hemorrhagic strokes. Within this group, the 30-day mortality rate for cases with IVC varies between 30–52%.[4,10] IVC is seen in 42–49% of cases with intracerebral hemorrhage and in approximately 15% of cases with subarachnoid hemorrhage.[11] The extension of intracerebral hemorrhage to the ventricle is thought to be an indicator of poor prognosis. In the prospective study conducted by Tuhrim et al., the presence of intraventricular component accompanying intracerebral hemorrhage and the significant effect of blood volume on 30-day mortality are mentioned.[12] Similarly, in the study of Young et al., intraventricular hemorrhage above 20 cc was associated with a poor prognosis. In addition, while addressing the relationship between hydrocephalus and poor outcome in their study, they mentioned that the application did not contribute to good prognosis in 8 of 9 cases who underwent EVD.[13] In our study we used Graeb index to determine the severity of ventricular hemorhage. According to the scoring system based on the calculation of the amount of blood in the ventricular system described by Graeb et al., more ventricular blood was evaluated to be associated with a worse prognosis. In addition, they reported that 90% of severe IVH patients ended with exitus.[14]

In cases with intraventricular hemorrhage, external ventricular drainage placement is frequently used as a standard surgical procedure in the presence of a worsening neurological score with signs of acute hydrocephalus and increased intracranial pressure. Despite problems such as the risk of occlusion and re-bleeding due to rapid intracranial pressure change in aneurysmal hemorrhages as well as catheter occlusion, the best treatment option for IVH is still seen as EVD placement.[15] In our clinic, EVD is placed in appropriate cases to prevent the development of acute hydrocephalus after IVH and to treat the symptoms of increased intracranial pressure.

In their study, Mracsko et al. addressed that intracranial blood triggered inflammatory processes and neuroinflammation evoked by intracerebral blood caused the activation of resident microglia, the infiltration of systemic immune cells and the production of cytokines, chemokines, extracellular proteases and reactive oxygen species.[9] The calculation of Neutrophil/Lymphocyte ratio is an easy and inexpensive method to reach as an inflammatory marker with complete blood count examination. In many studies, this ratio has also been used as a clinical outcome marker for cardiac events, ischemic stroke, chronic diseases, cancers and infectious diseases.[7,8]

A previous study revealed that high NLR values were significantly associated with 28-day post-traumatic mortality in the evaluation made within the first hour after admission in patients admitted to the emergency department after acute trauma.[16] Lee et al. argued that the high NLR value detected at the 6th hour following the admission to the emergency department in cases with severe head trauma was actually associated with a good prognosis due to the onset of the inflammatory process and perhaps recovery. In the same study, it was reported that the direct relationship found between high NLR and mortality in other studies was attributed to the uncertainty of the time interval between trauma and emergency department admission.[8] With these studies, Lee et al. pointed to a different result from many studies in the literature and our study.

In different studies conducted on the effect of NLR on survival in cases with intracerebral hemorrhage, NLR is frequently mentioned as a prognostic marker. In the review of 11 studies by Lattanzi et al., it is argued that NLR is a good prognostic marker for cases with intracerebral hematoma, which is a disease with a poor prognosis, usually followed by symptomatic treatments, and characterized by high mortality rates.[16] In a retrospective study conducted by Wang et al. on 224 patients with ISH, high NLR values measured the next day at admission were shown to be closely related to mortality. In similar studies, it is mentioned that the NLR value around

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7.35 is considered significant for differentiation between survival and mortality.[17,18] In our study, we evaluated the cases with IVH who underwent EVD, which is a more specific group among all ISH cases. Within this group, it was determined that the mean NLR value at admission for the surviving cases was 8.12, similar to other studies. For the patients who ended with exitus, the NLR values at admission were evaluated as statistically and significantly higher. However, in the statistical evaluation, the threshold value for well-being was found to be below 10.5.

As a result, NLR value is considered to be a parameter that can be used to predict the clinical course in IVH patients undergoing EVD. The small number of cases and the fact that the study was conducted retrospectively are the limitations of our study. Prospective studies to be conducted with more cases will be more useful in shedding light on the prognostic value of NLR.

Ethics committee approval

This study was conducted in accordance with the Declaration of Helsinki. For this study, the necessary permissions were obtained at the meeting of our hospital's Educational Planning Board (EPK) dated 26.03.2024.

Financial support

No financial support was received from any institution for the study.

Declaration of conflict of interest

The authors declare no conflict of interest regarding this article.

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