Dicle Tıp Dergisi / Dicle Med J (2025) 52 (1) : 1-6

www.diclemedj.org

Original Article / Özgün Araştırma

The effect of Lymphocyte Monocyte Ratio (LMR) on 30-day mortality of non-HCC post-transplant liver patients admitted to the intensive care unit

Vecihe Bayrak[1], Mehmet Çağatay Gürkök[2], Cihan Ağalar[3], Tarkan Ünek[3], Ferhan Demirer Aydemir[4], İrem Erdoğan Veziroğlu[5], Ali Necati Gökmen[6]

1 Nevsehir State Hospital, Intensive Care Department, Nevsehir, Turkey

2 Şanlıurfa Mehmet Akif İnan Education and Research Hospital, Intensive Care Department, Şanlıurfa, Turkey

3 Dokuz Eylul University General Surgery Department, İzmir, Turkey

4 Çanakkale State Hospital, Intensive Care Department, Çanakkale, Turkey

5 Nevsehir State Hospital, Internal Medicine Department Nevsehir, Turkey

6 Dokuz Eylül University Reanimation and Intensive Care Department İzmir, Turkey

Received: 03.10.2024; Revised: 29.01.2025; Accepted: 31.01.2025

Abstract

Aim: Our study aims to investigate the effect of the LMR value on the 30-day mortality and intensive care hospitalization days of post-transplant liver patients without hepatocellular cancer(HCC) admitted to the intensive care unit(ICU).

Methods: Our retrospective study included post-liver transplant patients in the ICU of Dokuz Eylul University Hospital between 2010 and 2020. We recorded patients' age, gender, aetiology of liver disease, donor type (living or deceased), duration of cold ischemia, scores, hospitalization days in the ICU, and 30-day mortality. LMR was calculated by dividing the patient's lymphocyte count by the monocyte count. Statistical analyses were performed using SPSS software version 24.0.

Results: 128 (92 male, 36 female) patients were included in our study. Twenty-four patients died within 30 days. The mean LMR was 1.498±2.134, and no significant difference existed between those with and without 30-day mortality (p=0.995). LMR value was not a predictor of mortality and ICU hospitalization days in these patients.

Conclusion: Our study revealed that LMR does not predict mortality or hospitalization days in post-liver transplant patients without HCC. The results of our study and previous studies suggest that LMR alteration is associated with an immune state produced by the tumour microenvironment. Our findings suggest that LMR may not be a valuable biomarker for predicting patient outcomes in post-liver transplant patients without HCC. However, this study provides a starting point for further investigation into the role of LMR in cancer diseases.

Keywords: Critical Care Medicine, Hematological changes, Liver failure, Viral hepatitis

DOI: 10.5798/dicletip.1657071

Correspondence / Yazışma Adresi: *Vecihe Bayrak, Nevsehir State Hospital, Intensive Care Department, Nevsehir, Turkey e-mail: vbayrak76@gmail.com*

Yoğun bakım ünitesine kabul edilen posttransplant nonHCC karaciğer hastalarında Lenfosit Monosit Oranının (LMR) 30 günlük mortalite üzerine etkisi

Öz

Amaç: Çalışmamızın amacı, lenfosit monosit oranının(LMR) , yoğun bakım ünitesine (YBÜ) kabul edilen HCC dışı karaciğer nakli sonrası hastaların 30 günlük mortalite ve yoğun bakım yatış süresi üzerine etkisini araştırmaktır.

Yöntemler: Retrospektif çalışmamıza, 2010-2020 yılları arasında Dokuz Eylül Üniversitesi Hastanesi YBÜ'nde karaciğer nakli sonrası hastalar dahil edildi. Hastaların yaşı, cinsiyeti, karaciğer hastalığının etiyolojisi, donör tipi (canlı donör/kadavra donör), soğuk iskemi süresi, skorları, YBÜ'de kalış süresi ve 30 günlük mortalite kaydedildi. LMR, hastanın lenfosit sayısının monosit sayısına bölünmesiyle hesaplandı. İstatistiksel analizler SPSS yazılım sürümü 24.0 kullanılarak yapıldı.

Sonuçlar: Çalışmamıza 128 (92 erkek, 36 kadın) hasta dahil edildi. 128 hastanın 24'ünde 30 gün içinde mortalite gelişti. LMR ortalaması 1.498±2.134 olup, 30 günlük mortalitesi olan ve olmayanlar arasında anlamlı bir fark yoktu (p=0.995). LMR değerinin bu hastalar için mortaliteyi belirleyici bir faktör olmadığı bulundu. Yoğun bakımda kalış süresi ile LMR arasında ilişki bulunamadı.

Sonuç: Çalışmamız, LMR'nin HCC olmayan karaciğer nakli sonrası hastalarda mortaliteyi veya hastaneye yatış günlerini öngörmediğini ortaya koydu. Çalışmamızın ve önceki çalışmaların sonuçları, LMR değişiminin tümör mikroçevresinin ürettiği bir bağışıklık durumu ile ilişkili olduğunu düşündürmektedir. Bulgularımız, LMR'nin, HCC'si olmayan karaciğer nakli sonrası hastalarda hasta sonuçlarını tahmin etmede değerli bir biyobelirteç olmayabileceğini göstermektedir. Ancak bu çalışma, LMR'nin kanser hastalıklarındaki rolüne ilişkin daha ileri araştırmalar için bir başlangıç noktası sağlamaktadır.

Anahtar kelimeler: Kritik hastalıklar tıbbı, hematolojik değişiklikler, karaciğer yetmezliği, viral hepatit.

INTRODUCTION

Estimating the prognosis of patients admitted to the intensive care unit (ICU) is essential for optimizing resource allocation and improving overall patient outcomes. In recent years, systemic inflammatory markers have attracted considerable attention as valuable tools for predicting clinical course and survival across a spectrum of diseases. Among these markers, the Lymphocyte-to-Monocyte Ratio (LMR) has gained prominence due to its utility in diverse clinical settings, including malignancies, cardiovascular diseases, and critically ill populations[1-3]. As an easily accessible and cost-effective parameter derived from a routine complete blood count, LMR reflects the balance between lymphocytes—key mediators of the adaptive immune response—and monocytes, which are integral components of inflammatory and innate immune pathways.

Within the field of hepatology, a robust body of evidence points to the prognostic significance of LMR in patients with hepatocellular carcinoma (HCC). Multiple studies have shown that LMR is inversely correlated with tumor aggressiveness and disease progression[4,5]. One of the few studies investigating the association of LMR with critically ill patients found that LMR was associated with longer hospital stay, 30-day mortality, and more renal replacement therapy[6]. There was also a study evaluating LMR as an inflammatory marker that may predict the prognosis of patients in the ICU[7].

Despite this extensive focus on HCC cohorts, there is a distinct knowledge gap regarding the role of LMR in non-HCC populations. Unraveling whether LMR can serve as a reliable predictor of short-term outcomes in these patients is paramount for clinicians seeking to optimize post-transplant management.

Accordingly, this study aims to evaluate the impact of LMR on short-term outcomes—specifically, 30-day mortality and ICU length of stay—in non-HCC post-liver transplant patients. Validating the role of LMR in non-HCC transplant recipients could ultimately help refine risk stratification models and support more personalized management strategies in the ICU setting.

METHODS

Our retrospective study focused on post-liver transplant patients at the ICU of Dokuz Eylül University Medical Faculty Hospital between 2010-2020. The study was approved by the non-interventional research ethics committee of Dokuz Eylül University Medical Faculty Hospital (Ethics Committee Approval Date: 30/03/2022, No: 2022/12-23).

Our hospital has a Hepatopancreaticobiliary Surgery and Liver Transplantation unit. Patients who consent to their data being used in studies must do so before the transplantation process, and their identities must be kept confidential. All patients included in our study provided consent.

1. Demographic and Clinical Data

A total of 128 patients were evaluated for this study. The demographic data, diagnoses, liver donor type, organ cold ischemia duration, ICU hospitalization days, and mortality within 30 days were obtained from their registered files.

2. Laboratory Data

Upon admission to the ICU after liver transplantation, blood samples were taken from the patients. Complete blood count, biochemistry, and coagulation tests were performed. The LMR was calculated by dividing the patient's lymphocyte count by the monocyte count.

3. Surgical procedure

The general surgery team at our hospital performed all transplants with the same coordinator using standard techniques.

4. Intensive Care

Patients who underwent liver transplantation (LT) were admitted to the ICU and followed up by an intensive care specialist. Immunosuppressive therapy was administered a predetermined protocol, initially using cyclosporine/tacrolimus, mycophenolate mofetil, and corticosteroids. If there was a possibility of renal toxicity, rapamycin inhibitors (everolimus, sirolimus) were used instead.

5. Statistics

Our study analyzed 128 patients undergoing liver transplantation (LT) in whom 30-day mortality was an important outcome. We also examined the length of stay in the ICU. Primary statistical methods included descriptive statistics, Mann-Whitney U test, and ANOVA, all performed using SPSS 24.0. Descriptive values were analyzed between the group with and without mortality at 30 days. Analysis was performed to determine the effect of LMR on 30-day mortality after LT. ANOVA was performed to assess whether LMR influenced ICU stay duration.

RESULTS

Our study included 128 patients (92 male, 36 female) with a mean age of 47.80±13.304 years. In our study group, the dominant cause of LT was hepatitis B virus cirrhosis (25%). Eighty-two (64.1%) transplants were from living donors, and 46 (35.9%) transplants were from deceased donors. Within 30 days, 24 of the 128 patients died.

The mean lymphocyte-to-monocyte ratio (LMR) was 1.498±2.134, and there was no significant

difference between those with and without 30-day mortality (p=0.995). One patient's monocyte count was zero, so the LMR value could not be calculated (Table 1).

Table I: Descriptive characteristics of patients and their association with mortality

	Survivors n=104		Non-survivors n=24		Total n =128		
	Mean	Sd	Mean	Sd	Mean	Sd	P
Age	46.9	13.26	51.67	13.064	47.80	13.304	0.080
Child Turcot Pugh Score	8.69	2.307	9.13	2.232	8.77	2.291	0.434
Lenfosit/ Monosit Ratio	1.479	2.262	1.585 n=23	1.462 n=23	1.498 n=127	2.134 n=127	.995
Cold İschemia Time (min)	283.81	235.176	277.25	202.306	282.58	228.636	0.939
WBC	9290.38	4907.821	9125	4815.58	9259.37	4872.249	0.819
Hb	10.451	1.6552	10.033	1.75	10.373	1.674	0.164
GFR	105.368	27.758	75.58	28.757	99.78	30.18	0
CRP	21.436	31.792	22.896	33.051	21.709	31.904	0.857
INR	1.783	0.3325	2.483	0.925	1.914	0.566	0
	n	%	n	%	n	%	
Gender							0.90
Male	75	72.1	17	70.8	92	71.9	
Female	29	27.9	7	29.2	36	28.1	
Type of Donor							0.764
Living	67	64.4	15	62.5	82	64.1	
Cadeveric	37	35.6	9	37.5	46	35.9	
Diagnosis							0.860
HBV cirrhosis	25	24	7	29.2	32	25	
HCV cirrhosis	5	4.8	1	4.2	6	4.7	
HBV+HDV	22	21.2	1	4.2	23	18	
Ethylic cirrhosis	14	13.5	3	12.5	17	13.3	
Autoimmune cirrhosis	3	2.9	2	8.3	5	3.9	
Acute Liver Failure	3	2.9	2	8.3	5	3.9	
Cryptogenic cirrhosis	16	15.4	5	20.8	21	16.4	
Biliary cirrhosis	5	4.8	1	4.2	6	4.7	
Others	11	10.6	2	8.3	13	10.2	
Blood Culture							
Unlabored	38	36.5	7	30.4	45	35.4	
Positive result	9	8.7	3	13	12	9.4	
Negative result	57	54.8	13	56.5	70	55.1	

** The Mann-Whitney U test calculated p-values. P-value < 0.05 was considered statistically significant. WBC: White blood cell CRP: C reactive protein Hb: Hemoglobin GFR: Glomerular filtration rate INR: International normal ratio HBV: Hepatitis B virus HCV: Hepatitis C virus HDV: Hepatitis D virus*

ROC analysis showed that LMR was not a good variable for explaining mortality. Since ROC was insignificant, range-median was used in univariate analysis (Table 2).

Table II: Analysis of LMR mean

	Range-Mean	p
LMR	(0-22) 5.27	>0,05 (0.986)

LMR: Lymphocyte monocyte ratio

Logistic regression analysis (Homer and Lemeshow Test) was performed to investigate the association between 30-day mortality and LMR in patients admitted to the ICU after liver transplantation. A p-value of 0.135612 was found, indicating that the LMR value was not a predictor of mortality for these patients.

In the analysis of the ICU hospitalization days (ANOVA), a p-value of 0.905 was found. There was no association between ICU hospitalization days and LMR.

DISCUSSION

Lymphocyte-to-monocyte ratio (LMR) has been extensively studied as a prognostic marker in various clinical settings, particularly in inflammatory diseases and malignancies. In our study, we investigated the predictive role of LMR in non-HCC liver transplant recipients regarding 30-day mortality and ICU hospitalization duration. Our findings indicate that LMR is not a significant predictor of early mortality or ICU length of stay in this patient population.

These results align with previous studies suggesting that LMR's prognostic utility may be limited to specific contexts, such as malignancy-related immune alterations[8-10]. While LMR has demonstrated prognostic significance in various malignancies, including pancreatic and gastric cancers, its role in non-malignant conditions appears less definitive. For instance, a meta-analysis of 1,795 patients demonstrated that an elevated LMR was associated with improved survival in pancreatic cancer patients[11]. Additionally, recurrence of hepatocellular carcinoma (HCC) after living donor liver transplantation has been associated with LMR[12].

A study examining LMR in liver transplant recipients with hepatocellular carcinoma (HCC) found that LMR was an independent predictor of survival[13]. This finding aligns with the hypothesis that LMR reflects the immune status of the tumor microenvironment, making it a more relevant prognostic marker in malignancy-related cases rather than in non-malignant conditions. Given that our study focused on non-HCC liver transplant recipients, the absence of a significant association between LMR and mortality may be attributed to the lack of an underlying tumor-driven immune response.

Our study has limitations related to LMR. The immune profile of LT patients undergoes significant changes due to immunosuppressive therapy, which can affect lymphocyte and monocyte counts. In addition, postoperative inflammatory responses, graft function and complications such as infections or rejection events also affect the change in immune cells. Since our aim was to investigate the prognostic markers for patients in ICU, the treatment that the patients received before coming to the ICU and possible conditions after transplantation make our study difficult. Our study was retrospective, limiting the ability to control for confounding variables that may have influenced the results. Conducting the study in a single center may reduce the generalizability of the findings to other transplant populations. Future research should focus on prospective multicenter studies with larger sample sizes to validate our findings and explore potential mechanisms underlying the observed differences in LMR's prognostic value.

The clinical implications of our study are twofold. First, LMR may not be a reliable prognostic marker for non-HCC patients after liver transplantation and highlights the need for alternative biomarkers. Second, our study and the above-mentioned results draw attention to the possibility that LMR may be associated with

a tumor-determined immune status. These results may be a clue that LMR should be further investigated in cancer diseases.

Ethics Committee Approval: The study was approved by the non-interventional research ethics committee of Dokuz Eylül University Medical Faculty Hospital (Ethics Committee Approval Date: 30/03/2022, No: 2022/12-23).

Conflict of Interest: The authors declared no conflicts of interest.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Qi X, Wang C, Shan X. Peripheral Blood Cell Ratios as Prognostic Predictors of Mortality in Patients with Hepatitis B Virus-Related Decompensated Cirrhosis. Clin Lab. 2021 Dec 1;67(12).

2. Dai K, Li Z, Luo Y, et all. The Predictive Value of the Monocyte-to-Lymphocyte Ratio and Monocyte-to-Haematocrit Ratio for Cardiac Rupture Patients with Acute Myocardial Infarction: A Propensity Score Matching Analysis. Risk Manag Health Policy. 2022 Jan 16;15:37-44.

3. Urbanowicz T, Olasińska-Wiśniewska A, Michalak M, et all. The Prognostic Significance of Neutrophil to Lymphocyte Ratio (NLR), Monocyte to Lymphocyte Ratio (MLR) and Platelet to Lymphocyte Ratio (PLR) on Long-Term Survival in Off-Pump Coronary Artery Bypass Grafting (OPCAB) Procedures. Biology (Basel). 2021 Dec 27;11(1):34.

4. Nouri-Vaskeh M, Mirza-Aghazadeh-Attari M, Pashazadeh F, et all. Prognostic Impact of Monocyte to Lymphocyte Ratio in Clinical Outcome of Patients with Hepatocellular Carcinoma: A Systematic Review and Meta-analysis. Galen Med J. 2020 Dec 25;9: e1948.

5. Song W, Tian C, Wang K et all. The pretreatment lymphocyte to monocyte ratio predicts clinical outcome for patients with hepatocellular carcinoma: A meta-analysis. Sci Rep. 2017 Apr 18;7:46601.

6. Li Y, Liu Y, Zhou C, et al. l. [Monocyte/lymphocyte ratio as a predictor of 30-day mortality and adverse events in critically ill patients: analysis of the MIMIC-III database]. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2021 May;33(5):582-6. Chinese.

7. Kalın BS, Özçaylak S, Solmaz İ, et all. Assessment of Risk Factors for Mortality in Patients in Medical Intensive Care Unit of a Tertiary Hospital. Indian J Crit Care Med. 2022 Jan;26(1):49-52.

8. Sato S, Shimizu T, Ishizuka M, et all. The preoperative pan-immune-inflammation value is a novel prognostic predictor for stage I-III colorectal cancer patients undergoing surgery. Surg Today. 2022 Jan 11.

9. Gao P, Peng W, Hu Y. Prognostic and clinicopathological significance of lymphocyte-to-monocyte ratio in patients with nasopharyngeal carcinoma. Head Neck. 2022 Mar;44(3):624-32.

10. Takamizawa S, Shimoi T, Satomi-Tsushita N, et all. Neutrophil-to-lymphocyte ratio as a prognostic factor for patients with metastatic or recurrent breast cancer treated using capecitabine: a retrospective study. BMC Cancer. 2022 Jan 14;22(1):64.

11. Li W, Tao L, Zhang L, Xiu D. Prognostic role of lymphocyte to monocyte ratio for patients with pancreatic cancer: a systematic review and meta-analysis. Onco Targets Ther. 2017 Jul 11;10:3391-7.

12. Kurihara T, Harada N, Morinaga A, et all. Predictive Factors for the Resectable Type of Hepatocellular Carcinoma Recurrence After Living Donor Liver Transplant. Transplant Proc. 2023 Jan-Feb;55(1):191-6.

13. Mano Y, Yoshizumi T, Yugawa K, et al. l. Lymphocyte-to-Monocyte Ratio Is a Predictor of Survival After Liver Transplantation for Hepatocellular Carcinoma. Liver Transpl. 2018 Nov;24(11):1603-11.