

Post-resection survival analysis in non-cirrhotic hepatocellular carcinoma based on preoperative PLR, NLR, and MxC values

Denny Krystian Tandi Ose^{1*}, Agi Satria Putranto¹

ABSTRACT

Background: To predict the prognosis of hepatocellular carcinoma (HCC), various staging systems have been developed, one of which is the Barcelona Clinic Liver Cancer (BCLC) staging system. However, this system has limitations in integrating systemic inflammatory markers that are relevant to tumor progression. Recent studies have shown that hematological parameters such as Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), and Monocyte \times C-reactive Protein (MxC) can serve as independent predictors of survival in non-cirrhotic HCC patients following resection.

Methods: A retrospective cohort study was conducted using secondary data. Preoperative laboratory parameters collected included PLR, NLR, and MxC values. Risk factors compared included age, gender, tumor size, tumor margin, and BCLC stage. Multivariate analysis was performed to identify survival predictors. Data were analyzed using SPSS version 25.

Results: A total of 59 subjects were included in the study. Eleven patients (18.5%) died, while 48 (81.4%) survived. Cut-off values to differentiate between high and low groups were 186.5 for PLR, 2.05 for NLR, and 1.11 for MxC. Bivariate analysis showed that high MxC ($p = 0.030$) and age >50 years ($p = 0.028$) were significantly associated with higher mortality risk. Subsequent multivariate analysis revealed that MxC was the strongest mortality predictor ($p = 0.05$, HR = 12.4, 95% CI: 1.56–99.14), indicating that patients with $MxC \geq 1.11$ were 12.4 times more likely to experience earlier mortality after resection.

Conclusion: Post-resection survival in non-cirrhotic hepatocellular carcinoma patients can be assessed using preoperative laboratory parameters and age. Elevated MxC values and age over 50 years may assist clinicians in predicting a higher risk of early mortality following surgical resection.

Keywords: Non-cirrhotic Hepatocellular Carcinoma, PLR, NLR, MxC, Survival.

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INTRODUCTION

Hepatocellular carcinoma (HCC) is the most common type of primary liver cancer, accounting for 75–85% of all liver cancer cases worldwide.¹⁻³ Various systems have been developed to predict HCC prognosis, one of which is the Barcelona Clinic Liver Cancer (BCLC) staging system.^{2,3} However, this system has limitations in integrating systemic inflammatory factors that are relevant to tumor progression. Recent studies on hematological parameters such as the Platelet-to-Lymphocyte Ratio (PLR), Neutrophil-to-Lymphocyte Ratio (NLR), and Monocyte \times C-reactive Protein (MxC) suggest their role as independent predictors for patient survival after resection of HCC.¹⁻⁵

A study by Zhang et al. demonstrated that PLR, NLR, and MxC values

significantly predicted overall survival (OS) in HCC patients.⁵ Patients with elevated ratios had worse prognosis, reflecting higher systemic inflammation and more likely advanced tumor stage.⁵ Validation using a nomogram showed better accuracy in predicting OS compared to conventional staging systems. Therefore, PLR, NLR, and MxC values may serve as simple, affordable, and reliable tools to guide the clinical management of HCC patients and support more personalized therapy strategies.

To date, there is no evidence that preoperative PLR, NLR, and MxC values influence postoperative survival in patients with non-cirrhotic HCC. This study aims to evaluate preoperative PLR, NLR, MxC, along with age, sex, tumor number, tumor margin, and BCLC stage as predictors of

postoperative survival in non-cirrhotic HCC patients.

METHODS

This retrospective cohort study was conducted at Cipto Mangunkusumo Hospital, Jakarta, from January 2020 to December 2024. The study used secondary data (hematological parameters, preoperative contrast-enhanced CT scans) obtained from medical records. The subjects included all patients with non-cirrhotic HCC who underwent hepatic resection and had complete data on hematologic parameters, multiphase abdominal contrast CT scans, and postoperative follow-up. Total sampling was used to determine the sample size.

Inclusion criteria included Radiological and clinical diagnosis of HCC, Treatment-

naïve patients, ECOG performance status 0–1, underwent curative resection, and non-cirrhotic liver based on laboratory and imaging screening for risk factors. Exclusion criteria included Patients with a histopathological diagnosis of intrahepatic cholangiocarcinoma (ICC) or combined HCC-ICC, Concurrent malignancies, Distant metastases, Postoperative survival less than one month, Blood sampling taken during active infection, Liver function Child-Pugh B or C, who received targeted therapy, immunotherapy, TACE, or HAIC prior to surgery.

Outcome measured: Survival status (alive or deceased), Preoperative hematologic values (PLR, NLR, MxC) measured within 7 days before surgery, Risk variables including age, sex, tumor margin, tumor size, and BCLC stage.

Statistical analysis: Univariable analysis was conducted to describe each variable (frequency and percentage). ROC analysis was used to determine cut-off values for PLR, NLR, and MxC based on the Youden Index. The Kaplan-Meier method and log-rank test were used to calculate and compare survival outcomes. The Proportional Hazard (PH) assumption was tested using goodness-of-fit (GOF). Variables meeting the PH assumption ($p > 0.05$) were analyzed with Cox proportional hazard regression; otherwise, Cox time-dependent regression was used. Multivariate analysis used backward stepwise Cox regression to determine significant predictors of postoperative mortality. A p -value < 0.05 was considered statistically significant.

Ethical approval was obtained from the Research Ethics Committee of Cipto Mangunkusumo Hospital, Universitas Indonesia. Statistical analysis was performed using SPSS version 25 for Windows.

RESULTS

The sample in this study consisted of 59 patients with hepatocellular carcinoma (HCC) who underwent liver resection at Cipto Mangunkusumo Hospital and had complete data on hematologic parameters and postoperative follow-up during the period from January 2020 to December 2024 (Table 1).

Table 1. Postoperative Characteristics of Hepatocellular Carcinoma Patients at Cipto Mangunkusumo Hospital (N=59)

| Variable | Frequency (n) | Percentages (%) |
|--------------------|---------------|-----------------|
| Age (Years) | | |
| ≤50 | 28 | 47.5 |
| >50 | 31 | 52.5 |
| Gender | | |
| Male | 31 | 52.5 |
| Female | 28 | 47.5 |
| Number of Tumors | | |
| Single | 42 | 71.2 |
| Multiple | 17 | 28.8 |
| Size of Tumor (cm) | | |
| ≤5 | 24 | 40.7 |
| >5 | 35 | 59.3 |
| BCLC Stage | | |
| A | 28 | 47.5 |
| B | 31 | 52.5 |
| PLR | | |
| Low (<186.5) | 46 | 78.0 |
| High (≥186.5) | 13 | 22.0 |
| NLR | | |
| Low (<2.05) | 29 | 49.2 |
| High (≥2.05) | 30 | 50.8 |
| MxC | | |
| Low (<1.11) | 28 | 47.5 |
| High (≥1.11) | 31 | 52.5 |

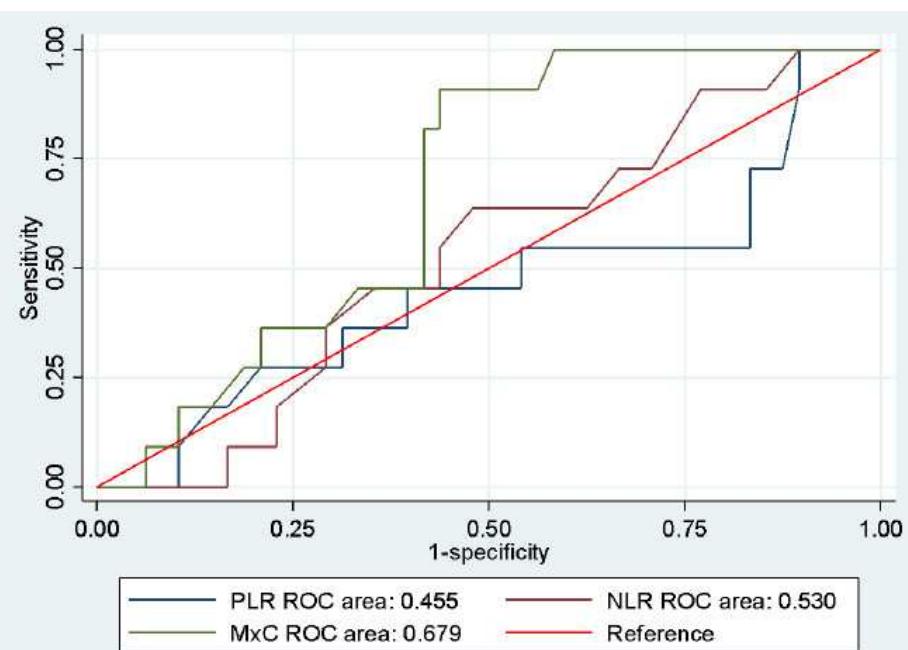


Figure 1. ROC Curves of PLR, NLR, and MxC for Predicting Postoperative Mortality in Patients with Hepatocellular Carcinoma.

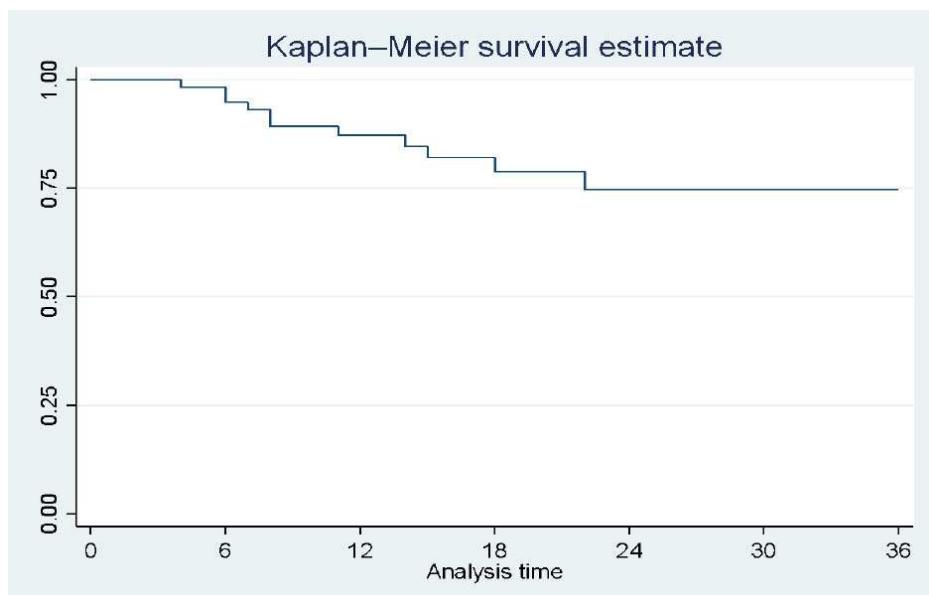
From Table 1, it was found that the majority of patients were in the >50 years age group (52.5%), male (52.5%), had a single tumor (71.2%), tumor size >5 cm (59.3%), BCLC stage B (52.5%), PLR <186.5 (78%), NLR ≥2.05 (50.8%), and MxC ≥1.11 (52.5%). The determination of cut-off points for the PLR, NLR, and

Table 2. Determination of Cut-Off Points for Parameters (PLR, NLR, MxC)

| Parameter | AUC (95%) | Youden Index | Cut-off |
|-----------|-----------------------|--------------|---------|
| PLR | 0.455 (0.252 – 0.658) | 0.064 | 186.5 |
| NLR | 0.530 (0.361 – 0.700) | 0.157 | 2.05 |
| MxC | 0.679 (0.540 – 0.818) | 0.472 | 1.11 |

Table 3. Postoperative Survival Status of Hepatocellular Carcinoma Patients at Cipto Mangunkusumo Hospital (N=59)

| Overall Survival (OS) | Frequency (n) | Percentage (%) |
|-----------------------|---------------|----------------|
| Deceased (Event) | 11 | 18.5 |
| Alive (Sensor) | 48 | 81.4 |

**Figure 2.** Kaplan-Meier Curve of Cumulative Overall Survival After Resection in Hepatocellular Carcinoma Patients.

MxC parameters was conducted using Receiver Operating Characteristic (ROC) analysis by evaluating the area under the curve (AUC) (Figure 1). The optimal cut-off point for each parameter was selected based on the highest Youden Index value.

In Table 2, the AUC value for PLR was 0.455, indicating that the ability of PLR to predict postoperative mortality in hepatocellular carcinoma patients falls into the poor classification category. Nevertheless, a cut-off point was still determined for PLR to allow for patient stratification, with the optimal cut-off value being 186.5 (Table 2). For NLR, the AUC was 0.530, suggesting a fair classification in predicting mortality, with the best cut-off point determined at 2.05. Meanwhile, the AUC for MxC was 0.679, which also falls into the fair classification category, with an optimal cut-off point of 1.11 (Table 2).

Patient survival was assessed based on two variables: survival status (alive or deceased) and length of survival (in months). The survival period was evaluated over a 3-year (36-month) follow-up duration (Table 3).

Table 3 shows that among hepatocellular carcinoma patients who underwent liver resection, 11 patients (18.5%) died, while 48 patients (81.4%) were still alive. The cumulative survival probability (Figure 2) represents the likelihood of a patient surviving over a specific period (36 months of observation), taking into account the entire time span. Survival probability ranges from 0 to 1, with 1 indicating a 100% chance of survival. The results showed that the cumulative overall survival (OS) probability in non-cirrhotic hepatocellular carcinoma patients gradually declined over time. At the end of the 36-month follow-up period,

the cumulative OS probability was 0.747 (74.7%). This means that by the end of the observation period, 74.7% of non-cirrhotic HCC patients who underwent resection were still alive. The median survival could not be calculated because fewer than 50% of the patients had died by the end of the observation period (Table 3 and Figure 2).

The survival profile of hepatocellular carcinoma patients according to influencing risk factors is presented in Table 4.

In Table 4, the cumulative survival probability was lower in the PLR ≥ 186.5 group compared to the PLR < 186.5 group (71.2% vs 77.1%). Similarly, patients with NLR ≥ 2.05 had a lower cumulative survival probability than those with NLR < 2.05 (67.9% vs 81.1%). For the MxC parameter, the cumulative survival probability was significantly lower in the MxC ≥ 1.11 group compared to the MxC < 1.11 group (54.3% vs 96.3%) (Table 4). The cumulative survival probability was also lower in patients aged > 50 years compared to those aged ≤ 50 years (57.7% vs 91%). Female patients had a slightly lower survival probability than male patients (73% vs 76.9%). Patients with single tumors had slightly lower survival than those with multiple tumors (74.7% vs 75.1%). In terms of tumor size, patients with tumors > 5 cm had lower survival than those with tumors ≤ 5 cm (74.9% vs 76.5%). Finally, patients with BCLC stage A had a slightly lower survival probability compared to those with stage B (75.0% vs 75.5%) (Table 4).

Before conducting the bivariate analysis, the proportional hazard (PH) assumption was assessed to determine whether any variables interacted with time—i.e., whether any variable had a hazard ratio that varied over time. The PH assumption was tested using the Goodness-of-Fit (GOF) test. A global test p-value greater than 0.05 indicates that the PH assumption is met (Table 5).

Based on Table 5, one variable—gender—did not meet the proportional hazard (PH) assumption (p-value > 0.05). Therefore, both the bivariate and multivariate analyses for gender were conducted using the Cox Extended/Cox Time-Dependent model. Based on the monthly survival and hazard curves, a

Table 4. Postoperative Survival in Hepatocellular Carcinoma Patients Based on Risk Factors at Cipto Mangunkusumo Hospital

| Variable | Mean Survival (Months) | Cumulative probability OS |
|-----------------------|------------------------|---------------------------|
| PLR | | |
| Low (<186,5) | 30 | 0.771 (0.579 – 0.883) |
| High ($\geq 186,5$) | 30 | 0.712 (0.334 – 0.900) |
| NLR | | |
| Low (<2,05) | 31 | 0.811 (0.561 – 0.927) |
| High ($\geq 2,05$) | 29 | 0.679 (0.399 – 0.849) |
| MxC | | |
| Low (<1,11) | 35 | 0.963 (0.764 – 0.995) |
| High ($\geq 1,11$) | 26 | 0.543 (0.289 – 0.740) |
| Age (Years) | | |
| ≤ 50 | 34 | 0.910 (0.677 – 0.977) |
| >50 | 26 | 0.577 (0.291 – 0.783) |
| Gender | | |
| Male | 32 | 0.769 (0.475 – 0.911) |
| Female | 29 | 0.730 (0.507 – 0.864) |
| Number of Tumors | | |
| Single | 31 | 0.747 (0.526 – 0.874) |
| Multiple | 24 | 0.751 (0.463 – 0.899) |
| Size Tumor (cm) | | |
| ≤ 5 | 30 | 0.765 (0.468 – 0.910) |
| >5 | 30 | 0.749 (0.531 – 0.876) |
| BCLC stage | | |
| A | 30 | 0.750 (0.479 – 0.894) |
| B | 30 | 0.755 (0.518 – 0.886) |

Table 5. Results of the Proportional Hazard (PH) Assumption Test

| Variable | Global Test (p-value) | Explanation |
|------------------|-----------------------|---------------------------------|
| PLR | 0.536 | Meets the PH assumption |
| NLR | 0.654 | Meets the PH assumption |
| MxC | 0.072 | Meets the PH assumption |
| Age | 0.606 | Meets the PH assumption |
| Gender | 0.025 | Does not meet the PH assumption |
| Number of Tumors | 0.220 | Meets the PH assumption |
| Size of Tumor | 0.882 | Meets the PH assumption |
| BCLC stage | 0.823 | Meets the PH assumption |

split time was set for the gender variable at $t \leq 12$ months, allowing the analysis to estimate separate hazard ratios before and after this time point (Table 5).

The purpose of the bivariate analysis was to examine the relationship between hematological parameters (PLR, NLR, MxC) and patient characteristics (age, gender, tumor number, tumor size, BCLC stage) with the dependent variable—postoperative survival or mortality in hepatocellular carcinoma patients. The results of the bivariate analysis are presented in Table 6.

Table 6 shows that for the PLR variable, the proportion of patients who experienced

the event (death) was higher in the PLR $\geq 186,5$ group (23.1%) compared to the PLR $< 186,5$ group (17.4%). However, Cox regression analysis showed no significant association between PLR and overall survival (OS) in hepatocellular carcinoma patients post-resection (p -value = 0.940, HR = 1.05, 95% CI: 0.28–3.40). For the NLR variable, the mortality rate was also higher in the NLR $\geq 2,05$ group (23.3%) compared to the NLR $< 2,05$ group (13.8%). Cox regression results again showed no significant association between NLR and OS (p -value = 0.393, HR = 1.71, 95% CI: 0.50–5.87). In contrast, for the MxC variable, the percentage of deaths was

markedly higher in the MxC $\geq 1,11$ group (32.3%) compared to the MxC $< 1,11$ group (3.6%). Cox regression analysis showed a significant association between MxC and OS (p -value = 0.030, HR = 9.82, 95% CI: 1.25–77.04). This indicates that patients with MxC $\geq 1,11$ had a 9.82 times higher risk of earlier death than those with MxC $< 1,11$ (Table 6).

Regarding age, mortality was higher in the >50 years group (29%) compared to those aged ≤ 50 years (7.1%). Cox regression revealed a significant association between age and OS (p -value = 0.028, HR = 5.79, 95% CI: 1.21–26.74), meaning patients older than 50 had a 5.69 times higher risk of dying earlier than younger patients. For the gender variable, more deaths occurred in female patients (25%) than male patients (12.9%). However, Cox regression showed no significant association between gender and OS (p -value = 0.078, HR = 6.72, 95% CI: 0.81–55.87).

Regarding tumor number, patients with multiple tumors had a higher mortality rate (23.5%) than those with single tumors (16.7%). However, this was not statistically significant (p -value = 0.548, HR = 1.46, 95% CI: 0.43–4.99). For tumor size, mortality was slightly higher in the >5 cm group (20%) compared to ≤ 5 cm (16.7%), with Cox regression showing no significant relationship (p -value = 0.908, HR = 0.93, 95% CI: 0.27–3.22). Finally, for the BCLC stage, the mortality rate was slightly higher in stage B (19.4%) compared to stage A (17.9%), but Cox regression found no significant association with OS (p -value = 0.944, HR = 0.96, 95% CI: 0.29–3.16) (Table 6).

Multivariate analysis was performed using a determinant modeling approach with a backward stepwise method, aiming to identify factors that significantly influenced postoperative overall survival (OS) in patients with hepatocellular carcinoma. The analysis used multiple Cox regressions. In the first step, all independent variables were included simultaneously with the dependent variable to construct the whole model, as shown in Table 7.

The next step involved the gradual elimination of variables, starting with those that had the highest p -values (>0.05), namely PLR, NLR, BCLC stage,

Table 6. Association Between Independent Variables and Postoperative Survival in Hepatocellular Carcinoma Patients at Cipto Mangunkusumo Hospital (N=59)

| Variable | OS HCC patients | | | | Total | p | HR | 95% CI |
|------------------|-----------------|------|----------|------|-------|-------|------|--------------|
| | Alive | | Deceased | | | | | |
| | n | % | n | % | | | | |
| PLR | | | | | | | | |
| Low (<186,5) | 38 | 82.6 | 8 | 17.4 | 46 | | Ref. | |
| High (≥186,5) | 10 | 76.9 | 3 | 23.1 | 13 | 0.940 | 1.05 | 0.28 – 3.40 |
| NLR | | | | | | | | |
| Low (<2,05) | 25 | 86.2 | 4 | 13.8 | 29 | | Ref. | |
| High (≥2,05) | 23 | 76.7 | 7 | 23.3 | 30 | 0.393 | 1.71 | 0.50 – 5.87 |
| MxC | | | | | | | | |
| Low (<1,11) | 27 | 96.4 | 1 | 3.6 | 28 | | Ref. | |
| High (≥1,11) | 21 | 67.7 | 10 | 32.3 | 31 | 0.030 | 9.82 | 1.25 – 77.04 |
| Age | | | | | | | | |
| ≤50 years | 26 | 92.9 | 2 | 7.1 | 28 | | Ref. | |
| >50 years | 22 | 71.0 | 9 | 29.0 | 31 | 0.028 | 5.69 | 1.21 – 26.74 |
| Gender | | | | | | | | |
| Male | 27 | 87.1 | 4 | 12.9 | 31 | | Ref. | |
| Female (t≤12) | 21 | 75.0 | 7 | 25.0 | 28 | 0.078 | 6.73 | 0.81 – 55.87 |
| Female (t>12) | | | | | | 0.364 | 0.35 | 0.04 – 3.38 |
| Number of Tumors | | | | | | | | |
| Single | 35 | 83.3 | 7 | 16.7 | 42 | | Ref. | |
| Multiple | 13 | 76.5 | 4 | 23.5 | 17 | 0.548 | 1.46 | 0.43 – 4.99 |
| Size of Tumor | | | | | | | | |
| ≤5 cm | 20 | 83.3 | 4 | 16.7 | 24 | | Ref. | |
| >5 cm | 28 | 80.0 | 7 | 20.0 | 35 | 0.908 | 0.93 | 0.27 – 3.22 |
| BCLC stage | | | | | | | | |
| A | 23 | 82.1 | 5 | 17.9 | 28 | | Ref. | |
| B | 25 | 80.6 | 6 | 19.4 | 31 | 0.944 | 0.96 | 0.29 – 3.16 |

tumor number, age, and tumor size. The elimination process was completed once no variables with p-values >0.05 remained, resulting in the final multivariate model presented in Table 8.

In Table 8, the final multivariate model identified MxC and age as significant predictors of postoperative survival in hepatocellular carcinoma patients (p-value < 0.05). Among these, MxC was the strongest factor influencing mortality. Patients with MxC ≥ 1.11 had a 12.44 times higher risk of earlier death compared to those with MxC <1.11, after adjusting for the gender variable (HR = 12.44, 95% CI: 1.56–99.14) (Table 8).

DISCUSSION

This study aimed to evaluate the role of preoperative PLR, NLR, and MxC values as survival predictors in patients with non-cirrhotic hepatocellular carcinoma (HCC) who underwent liver resection. Each of these parameters reflects different

aspects of systemic inflammation. Elevated NLR indicates a predominance of innate immune cells (neutrophils), which are pro-inflammatory and immunosuppressive toward lymphocytes, cells that play a key role in immunological tumor control.^{6–10} Furthermore, the MxC value is a relatively new but highly sensitive parameter for detecting active systemic inflammation. The main finding of this study is that a preoperative MxC value greater than 1.11 is significantly associated with postoperative mortality.

The initial step of the study involved determining the optimal cut-off values for each parameter. Based on ROC analysis and the Youden Index, the cut-off points were defined as follows: PLR at 186.5, NLR at 2.05, and MxC at 1.11. These thresholds are consistent with those found in other studies related to inflammatory markers in HCC. Although the AUC values of PLR and NLR were relatively low, we retained these parameters in the analysis

to allow stratification and comparison with previous literature. PLR and NLR are widely available, inexpensive, and have been shown to correlate with prognosis in other HCC settings. Their limited discriminatory power in this study likely reflects the non-cirrhotic population and relatively preserved liver function. Therefore, while their clinical utility may be limited here, including them provides valuable context for future validation.

In this study, postoperative survival outcomes showed that 11 patients (18.5%) died and 48 patients (81.4%) survived out of a total of 59. The cumulative overall survival (OS) probability was calculated at various time points (e.g., 4, 6, and 7 months). At month 4, the cumulative OS was 0.983 (98.3%) and gradually declined over time, reaching 0.747 (74.7%) at the end of the 36-month follow-up. This result aligns with previous research by Giannini et al. (2018), which reported 3-year survival rates ranging from 50% to

Table 7. Full Model of Factors Affecting Postoperative Survival in Hepatocellular Carcinoma Patients at Cipto Mangunkusumo Hospital (N=59)

| Variable | p | aHR | 95% CI |
|------------------------------|--------|-------|---------------|
| PLR | | | |
| Low (<186,5) | | Ref. | |
| High ($\geq 186,5$) | 0.690 | 1.44 | 0.25 – 8.54 |
| NLR | | | |
| Low (<2,05) | | Ref. | |
| High ($\geq 2,05$) | 0.503 | 0.60 | 0.14 – 2.66 |
| MxC | | | |
| Low (<1,11) | | Ref. | |
| High ($\geq 1,11$) | 0.054 | 12.06 | 0.96 – 151.90 |
| Age | | | |
| ≤ 50 years | | Ref. | |
| >50 years | 0.109 | 4.65 | 0.71 – 30.51 |
| Gender | | | |
| Male | | Ref. | |
| Female ($t \leq 12$ months) | 0.011* | 21.0 | 2.03 – 217.07 |
| Female ($t > 12$ months) | 0.935 | 1.11 | 0.09 – 13.61 |
| Number of Tumors | | | |
| Single | | Ref. | |
| Multiple | 0.320 | 2.14 | 0.48 – 9.57 |
| Size of Tumor | | | |
| ≤ 5 cm | | Ref. | |
| >5 cm | 0.068 | 0.22 | 0.04 – 1.12 |
| BCLC stage | | | |
| A | | Ref. | |
| B | 0.476 | 1.64 | 0.42 – 6.34 |

*Statistically significant if p-value is less than 0.05

Table 8. Final Model of Factors Affecting Postoperative Survival in Hepatocellular Carcinoma Patients at Cipto Mangunkusumo Hospital (N=59)

| Variable | p | aHR | 95% CI |
|------------------------------|--------|-------|--------------|
| MxC | | | |
| Low (<1.11) | | Ref. | |
| High (≥ 1.11) | 0.017* | 12.44 | 1.56 – 99.14 |
| Gender | | | |
| Male | | Ref. | |
| Female ($t \leq 12$ months) | 0.031* | 10.31 | 1.23 – 86.32 |
| Female ($t > 12$ months) | 0.699 | 0.64 | 0.06 – 6.27 |

*Statistically significant if p-value is less than 0.05

70% in patients with non-cirrhotic HCC. In terms of survival distribution based on risk factors, the cumulative survival probabilities were lower in patients with PLR ≥ 186.5 , NLR ≥ 2.05 , MxC ≥ 1.11 , age > 50 years, female gender, single tumors, tumor size > 5 cm, and BCLC stage A. The violation of the proportional hazard assumption for gender indicated a time-dependent effect, with female patients showing higher mortality within the first 12 months. This could reflect biological differences in hormonal milieu, tumor

biology, or treatment tolerance, although it may also represent a statistical artifact given the limited sample size. Larger studies are warranted to clarify whether this observation holds clinical significance.

Bivariate analysis showed a significant association ($p < 0.05$) between high MxC values and postoperative mortality (p -value = 0.030). Non-cirrhotic HCC patients with MxC ≥ 1.11 had a 9.82-fold increased risk of death compared to those with MxC < 1.11 . In contrast, PLR and NLR were not significantly associated with

survival, with p -values of 0.940 and 0.393, respectively. This may be due to the early-stage condition of non-cirrhotic HCC patients, where the systemic inflammatory response has not yet become severe.⁷⁻¹¹ Moreover, in non-cirrhotic conditions, immune dysfunction is less prominent due to better-preserved liver function. As a result, the balance between innate and adaptive immunity—as represented by neutrophil and lymphocyte levels—may not be markedly altered. This likely explains why PLR and NLR were not dominant predictors of survival in this study.^{1,5,11-15}

These findings are consistent with a previous study, which also showed that elevated MxC was associated with lower OS.¹⁶ MxC is considered a pure inflammatory marker that is not influenced by liver fibrosis, thus offering a potentially stronger prognostic value. High MxC levels are associated with increased recurrence, lower survival rates, and a more aggressive tumor microenvironment. Among the risk factors, age was found to be significantly associated with mortality ($p < 0.05$). The proportion of deaths was higher in patients aged > 50 years (29%) (p -value = 0.028, HR = 5.79, 95% CI: 1.21–26.74). Patients over 50 years old had a 5.69-fold higher risk of death compared to those aged ≤ 50 years. This may be explained by the increased risk of comorbidities and limited treatment options in older patients due to anesthesia risks and potential complications. No significant associations with mortality were found for gender, tumor number, tumor size, or BCLC stage. Although MxC emerged as the most robust predictor in our analysis, it remains a relatively novel marker with limited validation. Its prognostic role needs to be confirmed through larger multicenter studies and prospective trials. Integration with established inflammatory ratios and imaging parameters would help establish its reproducibility and clinical applicability.

From the data analysis, it was found that patients with high inflammatory ratios had a substantially higher mortality risk than those with low ratios. This is consistent with previous studies, which showed that inflammation-based scores such as NLR and CRP were strongly correlated with

survival in HCC patients.^{14,17} Moreover, a previous study also stated that nearly all systemic inflammatory scores—whether two-parameter or multi-parameter—play a significant role in determining survival outcomes in resected HCC patients.¹⁴

One of the major advantages of using NLR, PLR, and MxC is their ease of application in clinical settings.¹⁴⁻¹⁸ All components are derived from routine, low-cost laboratory tests that are widely available in most healthcare facilities. This makes them practical tools for preoperative risk stratification, especially in resource-limited settings. In addition to serving as survival assessment tools, NLR, PLR, and MxC may also help determine perioperative strategies. For instance, patients with high ratios could be placed under intensive monitoring, receive more aggressive nutritional support, and undergo systemic optimization prior to surgery.

However, this study has some limitations. First, the relatively small sample size and single-center design may limit the external validity of the results. Future multicenter studies with larger and more diverse populations are needed to confirm these findings and improve generalizability. This study did not adjust for potential confounders such as comorbidities, perioperative complications, or adjuvant therapies, which may have influenced survival outcomes. Future research should incorporate these variables to provide a more comprehensive risk adjustment.

CONCLUSION

Based on the findings of this study, it can be concluded that preoperative MxC is a significant predictor of postoperative survival in patients with non-cirrhotic hepatocellular carcinoma who undergo liver resection. Patients with higher MxC values are at increased risk of mortality compared to those with lower values, indicating that systemic inflammation significantly impacts postoperative outcomes. It is recommended that future research include multiple centers or hospitals to obtain a more diverse and larger sample size for more robust statistical analysis. Additional clinical variables could also be incorporated to assess the

contributing factors comprehensively. The use of MxC should be considered in clinical algorithms as a risk and prognostic predictor, especially in populations with limited access to advanced imaging technologies.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding this study.

ETHICS CONSIDERATION

Ethical approval for this study was obtained from the Research Ethics Committee of Cipto Mangunkusumo Hospital, Universitas Indonesia. Due to the retrospective design, individual informed consent was waived/received according to institutional guidelines.

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AUTHOR CONTRIBUTIONS

DKTO conceived the study, performed data collection, and drafted the manuscript. ASP contributed to data analysis, interpretation, and critical revision of the manuscript. Both authors read and approved the final version of the manuscript.

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