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Value of Inflammatory Scores in the Assessment of the Prognosis of Hepatocellular Carcinoma (HCC) during Hospitalization, in Internal Medicine Department of University Hospital Centre of Bouake

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Abstract

Background and aim: Hepatocellular carcinoma (HCC) is one of the leading causes of death in Africa. Many inflammatory scores have been used to predict the prognosis of this disease in various situations. The aim of this study was to determine the influence of NLR, PLR and SII on the prognosis of advanced HCC in hospitalized patients. **Materials and methods:** It was a cross-sectional analytical study carried out in the Internal Medicine Department of Bouake University Hospital over a period of 3 years. **Results:** Out of 96 patients included in the study, we found a significant association between SII and CHILD score ≥ B. We also identified NLR as an independent predictor of hepatic encephalopathy. **Conclusion:** This study shows the relationship between inflammatory scores and hepatic insufficiency and the possibility of using NLR to predict in-hospital hepatic encephalopathy in patients suffering from advanced HCC.

Keywords

Inflammation Score, Hepatocellular Carcinoma, Prognosis, West Africa

1. Introduction

Hepatocellular carcinoma (HCC) is a public health problem. According to the Global Cancer Observatory (Globocan), in 2022, HCC was the fourth most common cancer in Africa, behind breast, cervical and prostate cancer, with 7,3844 new cases and 70,315 deaths [1]. In sub-Saharan Africa, HCC occurs mainly in young men infected by viral hepatitis B, the major risk factor of this disease [2], which is particularly transmitted during childhood and pregnancy. The current challenge for WHO member states is the reduction of hepatitis-related mortality of 65% and new infections of 90% by 2030, [3], only achievable by vaccination against viral hepatitis B. However, low socio-economic status of patients could be a significant obstacle because of low health literacy of patients, and limited healthcare resources and access, including lack of insurance or ability to pay for care [4]. Beyond prevention, the assessment of the prognosis of HCC has evolved in recent years, probably because of a better understanding of the relationship between cancer and inflammation.

Inflammation is common in HCC and contributes to the poor prognosis of the disease [5]. It can precede development of malignancy or may be the consequence of oncogenic change that drives a tumor-promoting inflammatory milieu, stimulating angiogenesis, metastasis, subverts adaptive immunity and alters response to treatment. [6]. Thus, inflammation-based scores have been used as cost-effective biomarkers for diagnosis and assessment of prognosis of digestif [7] [8] and extra-digestive cancers [9]-[11]. In HCC, elevated neutrophil to lymphocyte ratio (NLR) [12], platelet-to-lymphocyte ratio (PLR) [13], Systemic Inflammation Index (SII) [14], aspartate aminotransferase to lymphocyte ratio index (ALRI) [15], or Prognostic nutritional index (PNI) [16] before treatment, have been correlated with a poor prognosis in patients after curative or palliative treatment, with a relative superiority of NLR over PLR, ALRI, and SII in Trans-arterial chimioembolisation (TACE) [17]. In sub-Saharan Africa, few studies focused on inflammatory scores in the assessment of HCC's prognosis especially for in-hospital patients.

The aim of this study was to determine the influence of NLR, LPR and SII on the prognosis of advanced HCC in hospitalized patients.

2. Materials and Methods

2.1. Study Design

This was a cross-sectional analytical study carried out in the Internal Medicine Department of Bouake University Hospital over a period of 3 years, from 1 January 2020 to 31 December 2022.

2.2. Patients

Inclusion criteria: patient aged 14 years old or more with advanced HCC. Advanced HCC was HCC at stage C or D of Barcelona Clinic Liver Classification. The diagnosis of HCC was done if one of the following conditions were fulfilled:

- presence of hepatic nodule on a cirrhotic liver with wash-in wash-out vascular kinetics on abdominal CT;
- patients with a hepatic nodule or mass on a cirrhotic liver with evidence of portal thrombosis on ultrasound or abdominal CT;
- all patients with histologically confirmed HCC in non-cirrhotic liver with or without significant elevation of AFP. The normal adult value was less than 20 ng/ml. An AFP level ≥ 400 ng/ml was considered significant but a level < 400 ng/ml did not rule out the diagnosis.

Exclusion criteria: patients with viral or bacterial infection, including ascites fluid infection, and patients treated with anti-inflammatory drugs were not included in the study. Also, incomplete records for the studied parameters were not included.

2.3. Baseline Characteristics

We collected sociodemographic, clinical, biological and radiological characteristics of patients on a standardized survey form (**Appendix 1**). Blood count, was used to calculate inflammatory scores by the following formulas:

- **NLR** was the ratio of absolute neutrophil and lymphocyte values
- **PLR** was the ratio of platelet rate and absolute lymphocyte value
- **SII** was determined by the formula, SII = (P × N)/L, where L, N and P represent lymphocyte, neutrophil and platelet counts respectively.

The cut-off of NLR, PLR and SII were chosen according to their significance in systematic review and meta-analysis. We also considered the race and ethnicity of patients to choose these cut-off.

2.4. Data Source

All the data of this study came from the medical records of the patients.

2.5. Statistical Analysis

Statistical analysis was performed using Epi-info 7 software.

Data were processed and analyzed using epi info7 software. Word and Excel were used for graphical representations. Quantitative variables were expressed as median or mean with extremes, and qualitative variables were expressed as proportion. The Chi-square test was used to find a relationship between the categorical variables. When the expected number of participants was less than 5, the Fisher test was applied. The significance level was less than 5% for univariate analyses.

After descriptive analysis of our data, we performed univariate analysis and if association were found between variables, a multivariate analysis was performed. we firstly analyzed the influence of sociodemographic (age, sex) and morphological characteristics of HCC (number and size of nodules) on inflammatory scores. Then we assessed the influence of inflammatory scores (NLR, PLR, SII scores) on the following prognostic data such as liver function (hepatic encephalopathy,

child score), death, length of stay, performans status and BCLC stage.

2.6. Ethics Statement

The study was conducted in accordance with the ethical guidelines of the 1975 Declaration of Helsinki (6th revision, 2008). All data were anonymized during the study process and kept confidentially within the Internal Medecine Department

The study was conducted in accordance with the principles of the Declaration of Helsinki.

3. Results

Out of 160 HCC patients, 96 patients met the criteria and were included in the study**.** Sixty-four patients were excluded from the study, including 47 for ascites infection and 17 patients for incomplete data. The mean age was 48.1 ± 15 years and the sex ratio was 3.7. The educational level was absent (31%), primary (46%), secondary (17%) and university (6%). HCC was classified as BCLC C in 55% of cases and BCLC D in 45%. The mean length of stay was 4.5 ± 4.8 days. The means of inflammatory scores were 4.02 ± 2.97 (NLR), 163.9 ± 133.8 (PLR) and 1004.6 ± 1068 (SII) as shown in Table 1.

Table 1. Mean of neutrophils, lymphocytes, platelets count and inflammation scores in the 96 patients.

Parameters	Means
Neutrophils (cells/mL)	5900 ± 3400 (9000; 21800)
Lymphocytes(cells/mL)	1800 ± 1100 (500; 8600)
Platelets (cells/mL)	235700 ± 132700 (19000; 565000)
NLR	4.02 ± 2.97 (0.01; 17.45)
PLR	163.9 ± 133.8 (12.8; 929.4)
SII	1004.6 ± 1068.8 (2.3; 8271.8)

PLR, was significantly associated with age (RR = 1.64; CI 95: 1.24; 2.17). There was no association between inflammatory scores and sex, size and number of hepatic nodules (Table 2).

Table 2. Influence of age, sex, number and size of nodules on inflammation scores.

	NLR	PLR	SII
	7 (33.3%)	**3 (14.3%)**	5 (23.8%)
Age > 65	1.11 (0.7; 1.5)	**1.64 (1.24; 2.17)**	1.3 (0.99; 1.85)
	0.057	**0.005**	0.09
male	32 (43.84%)	30 (76.9%)	32 (43.8%)
gender	1.39 (1.03; 1.87)	1.06 (0.5; 2.21)	1.31 (0.95; 1.80)
	0.05	0.86	0.12

Continued

	26 (41.9%)	25 (40.3%)	25 (40.3%)
Multiples nodules	1.16 (0.85; 1.59)	0.98 (0.69; 1.39)	1.03 (0.74; 1.44)
	0.35	0.93	0.84
	10 (66.7%)	19 (47.5%)	15 (37.5%)
Nodule size > 3 cm	1.32 (0.90; 1.93)	0.78 (0.45; 1.36)	1.12 (0.59; 2.11)
	0.07	0.44	0.69

Mortality was 18.7%. No association was found between inflammation scores and death in patients hospitalized for more than 5 days. In univariate analysis, NLR and SII were respectively identified as risk factors for hepatic encephalopathy (RR = 1.49; CI 95: 1.1; 2.01) and CHILD ≥ B score (RR = 3.93; CI 95: 1.24; 12.4). In multivariate analysis, NLR alone was identified as an independent predictor of hepatic encephalopathy (Table 3).

Table 3. Association between inflammation scores and prognostic factors in advanced HCC.

	Death	Length of stay ≥5j	Encephalo-pathy	Child score ≥ B	PS ≥ 3	BCLCD
NLR (n)						
≥4 (37)	9 (24.3%)	26 (70.3%)	16 (43.2%)	32 (86.5%)	19 (51.3%)	18 (48.6%)
RR*	1.1 (0.90; 1.38)	0.91 (0.47; 1.74)	1.49 (1.1; 2.01)	2 (0.80; 5.1)	1.1 (0.74; 1.67)	1.15 (0.79; 1.68)
p	0.26	0.78	**0.002**	0.11	0.59	0.44
aOR*			**3.90 (1.37; 11.15)**			
p			**0.01**			
PLR (n)						
≥164 (39)	9 (23.1%)	31 (79.5%)	12 (30.8%)	33 (84.6%)	18 (46.1%)	17 (43.6%)
RR	1.09 (0.89; 1.34)	1.93 (0.74; 5.02)	1.11 (0.86; 1.43)	1.71 (0.72; 4.1)	0.94 (0.64; 1.39)	0.99 (0.69; 1.42)
p	0.36	0.17	3.90	0.20	0.77	0.97
SII (n)						
≥1004 (39)	8 (21.1%)	31 (81.6%)	14 (36.8%)	35 (92.1%)	19 (50%)	18 (47.4%)
RR	1.04 (0.85; 1.28)	1.87 (0.87; 3.9)	1.28 (0.97; 1.68)	**3.93 (1.24; 12.4)**	1.06 (0.71; 1.6)	1.11 (0.76; 1.61)
p	0.63	0.08	0.05	**0.007**	0.74	0.56
aOR				3.78 (0.96; 14.85)		
p				0.05		

RR: risk ratio (univariate analysis); aOR: Adjusted Odds Ratio (multivariate analysis); p value; *PS = Performans status.

4. Discussion

4.1. Epidemiological Characteristics

Over 96 patients included in our study, 45% were at end-stage of HCC. Our results were similar to those of Pkossou (40.3%) [18], but significantly lower than those of Pantong in Nigeria (61.43%) [19], certainly due to the large number of HIV-infected patients in his study. In fact, HIV infection is associated with a faster clinical presentation and shorter survival [19]. HCC occurred predominantly in young men (48.1 years) and more than 70% of patients had a low level of education. Our results were comparable to those of Diallo in Senegal (47 years) [20], and Bekolo in Cameroon who reported a mean age of 51.8 years in a sample of more than 900 patients [21]. Both authors observed male predominance. Another author noted a low level of education [22].

4.2. Inflammatory Scores and Neutrophil, Lymphocyte and Platelet Count

In our study, the means of inflammatory scores were 4.02 ± 2.97 (NLR), 163.9 ± 133.8 (PLR) and 1004.6 ± 1068 (SII), and were superior to the cut-off of NLR, PLR and SII required to predict cancer prognosis in the literature. In the study of Zhang [8], RNL was 2.1, RPL and SII were respectively 139.5 and 438.7. This study was about gastric cancer and was not carried out in Africa. But, another study was done in Ivory coast and showed lower inflammatory scores (NLR > 2.5 and PLR > 92) [23]. In this study, patients at intermediate stage of HCC were also included. Moreover, lymphocyte count was higher (1881 vs 1800), while platelet (168000 vs 235000) and neutrophil count (4153 vs 5900) were lower. Thus, the lower lymphocyte count versus higher platelet and neutrophil count of our patients matched with their advanced stage of HCC and performans status (PS ≥ 3), although no statistical association was found between inflammatory scores, PS and BCLC D. In fact, B cells limits the growth of hepatic tumors and T cells prevents the initial steps carcinogenesis [24], whereas neutrophils have been shown to be a poor prognostic factor by promoting the development of HCC through p53 and STAT3 signaling pathways [25] and platelets facilitate the tumor cells invasion **[26]**.

4.3. Inflammatory Scores and Sociodemographic and Morphological Characteristics

In our study, PLR was significantly higher in elderly patients**.** In the elderly, especially in the case of pathological aging, there is a dysregulation of the immune system which may be responsible for chronic inflammation [27]**.** No association was found between inflammatory scores and number or tumor size**.** However, this association was described for the number and size of tumors. In fact, in a study carried out over 1000 patients, NLR was only associated with tumor size ≥ 2 cm, while PLR was significantly associated with tumor size ≥ 2 cm with a strong association with tumor size > 3 cm [28]. In addition, a recent meta-analysis suggested

a significant association between increased SII, multiple tumor numbers (OR = 1.42, 95% CI = 1.09 - 1.85, p = 0.009) and maximum tumor diameter > 5 cm (OR = 3.06, 95% CI = 1.76 - 5.30, p < 0.001), without association with sex.

4.4. Inflammatory Scores and Liver Function

In our study, an increased SII was associated with altered liver function (CHILD score ≥B), and NLR was identified as independent predictor of hepatic encephalopathy. The relationship between inflammation and liver function is well known. Indeed, inflammation was associated with both the presence and severity of hepatic encephalopathy [29]. Moreover, NLR at discharge was identified as a significant predictor of 30-, 90- and 180-day readmissions in patients with hepatic encephalopathy [30].

4.5. Inflammatory Scores and in-Hospital Survival

No association was found between inflammatory scores and death. In several studies, inflammation score were significantly associated with poor prognosis, during the follow-up after curative or palliative treatment [31] [32].

5. Limitation of the Study

Our study was cross-sectional and based on medical records. It is possible that there may be information bias, particularly concerning the use of anti-inflammatory treatments, which is frequent in our patients. Nevertheless, all patients with infections were excluded from the study.

6. Conclusion

This study demonstrates the influence of age on inflammatory score. It also shows the relationship between inflammatory scores and hepatic insufficiency and the possibility to use NLR to predict in-hospital hepatic encephalopathy on patients suffering from advanced HCC. A prospective study may give more information about these findings.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Ferlay, J., Lam, F., Laversanne, M., Colombet, M., Mery, L., Piñeros, M., *et al.* (2022) Global Cancer Observatory: Cancer Today. https://gco.iarc.who.int/today

[2] Yang, J.D., Hainaut, P., Gores, G.J., Amadou, A., Plymoth, A. and Roberts, L.R. (2019) A Global View of Hepatocellular Carcinoma: Trends, Risk, Prevention and Management. *Nature Reviews Gastroenterology & Hepatology*, **16**, 589-604.

https://doi.org/10.1038/s41575-019-0186-y

[3] Cooke, G.S., Andrieux-Meyer, I., Applegate, T.L., Atun, R., Burry, J.R., Cheinquer, H., *et al*. (2019) Accelerating the Elimination of Viral Hepatitis: A Lancet Gastroenterology & Hepatology Commission. *The Lancet Gastroenterology & Hepatology*, **4**, 135-184. https://doi.org/10.1016/s2468-1253(18)30270-x

[4] Gnyawali, B., Pusateri, A., Nickerson, A., Jalil, S. and Mumtaz, K. (2022) Epidemiologic and Socioeconomic Factors Impacting Hepatitis B Virus and Related Hepatocellular Carcinoma. *World Journal of Gastroenterology*, **28**, 3793-3802. https://doi.org/10.3748/wjg.v28.i29.3793

[5] Yang, Y., Kim, S. and Seki, E. (2019) Inflammation and Liver Cancer: Molecular Mechanisms and Therapeutic Targets. *Seminars in Liver Disease*, **39**, 26-42. https://doi.org/10.1055/s-0038-1676806

[6] Candido, J. and Hagemann, T. (2012) Cancer-Related Inflammation. *Journal of Clinical Immunology*, **33**, 79-84. https://doi.org/10.1007/s10875-012-9847-0

[7] Qi, Q., Zhuang, L., Shen, Y., Geng, Y., Yu, S., Chen, H., *et al*. (2016) A Novel Systemic Inflammation Response Index (SIRI) for Predicting the Survival of Patients with Pancreatic Cancer after Chemotherapy. *Cancer*, **122**, 2158-2167. https://doi.org/10.1002/cncr.30057

[8] Stevens, L., Pathak, S., Nunes, Q.M., Pandanaboyana, S., Macutkiewicz, C., Smart, N., *et al*. (2015) Prognostic Significance of Pre-Operative C-Reactive Protein and the Neutrophil-Lymphocyte Ratio in Resectable Pancreatic Cancer: A Systematic Review. *HPB*, **17**, 285-291. https://doi.org/10.1111/hpb.12355

[9] Szkandera, J., Absenger, G., Liegl-Atzwanger, B., Pichler, M., Stotz, M., Samonigg, H., *et al*. (2013) Elevated Preoperative Neutrophil/Lymphocyte Ratio Is Associated with Poor Prognosis in Soft-Tissue Sarcoma Patients. *British Journal of Cancer*, **108**, 1677-1683. https://doi.org/10.1038/bjc.2013.135

[10] Mandaliya, H., Jones, M., Oldmeadow, C. and Nordman, I.I.C. (2019) Prognostic Biomarkers in Stage IV Non-Small Cell Lung Cancer (NSCLC): Neutrophil to Lymphocyte Ratio (NLR), Lymphocyte to Monocyte Ratio (LMR), Platelet to Lymphocyte Ratio (PLR) and Advanced Lung Cancer Inflammation Index (ALI). *Translational Lung Cancer Research*, **8**, 886-894. https://doi.org/10.21037/tlcr.2019.11.16

[11] Murri, A.M.A., Bartlett, J.M.S., Canney, P.A., Doughty, J.C., Wilson, C. and McMillan, D.C. (2006) Evaluation of an Inflammation-Based Prognostic Score (GPS) in Patients with Metastatic Breast Cancer. *British Journal of Cancer*, **94**, 227-230. https://doi.org/10.1038/sj.bjc.6602922

[12] Xiao, W., Chen, D., Li, S., Fu, S., Peng, B. and Liang, L. (2014) Prognostic Significance of Neutrophil-Lymphocyte Ratio in Hepatocellular Carcinoma: A Meta-Analysis. *BMC Cancer*, **14**, Article No. 117. https://doi.org/10.1186/1471-2407-14-117

[13] Lin, W., Zhong, M., Zhang, Y., Wang, H., Zhao, H., Cheng, B., *et al*. (2018) Prognostic Role of Platelet-To-Lymphocyte Ratio in Hepatocellular Carcinoma with Different BCLC Stages: A Systematic Review and Meta-analysis. *Gastroenterology Research and Practice*, **2018**, Article ID: 5670949. https://doi.org/10.1155/2018/5670949

[14] Xu, L., Yu, S., Zhuang, L., Wang, P., Shen, Y., Lin, J., *et al*. (2017) Systemic Inflammation Response Index (SIRI) Predicts Prognosis in Hepatocellular Carcinoma Patients. *Oncotarget*, **8**, 34954-34960. https://doi.org/10.18632/oncotarget.16865

[15] Jin, J., Zhu, P., Liao, Y., Li, J., Liao, W. and He, S. (2015) Elevated Preoperative Aspartate Aminotransferase to Lymphocyte Ratio Index as an Independent Prognostic Factor for Patients with Hepatocellular Carcinoma after Hepatic Resection. *Oncotarget*, **6**, 19217-19227. https://doi.org/10.18632/oncotarget.4265

[16] Wang, D., Hu, X., Xiao, L., Long, G., Yao, L., Wang, Z., *et al*. (2021) Prognostic Nutritional Index and Systemic Immune-Inflammation Index Predict the Prognosis of Patients with HCC. *Journal of Gastrointestinal Surgery*, **25**, 421-427. https://doi.org/10.1007/s11605-019-04492-7

[17] Young, S., Cam, I., Gencturk, M., Rubin, N., D'souza, D., Flanagan, S., *et al*. (2021) Inflammatory Scores: Comparison and Utility in HCC Patients Undergoing Transarterial Chemoembolization in a North American Cohort. *Journal of Hepatocellular Carcinoma*, **8**, 1513-1524. https://doi.org/10.2147/jhc.s335183

[18] Kpossou, A.R., Vignon, R.K., Sokpon, C.N.M., Hounssou, E.F. and Gnangnon, F.H.R. (2021) Prise en charge thérapeutique des carcinomes hépatocellulaires au Centre National Hospitalier Universitaire Hubert Koutoukou Maga de Cotonou. *Médecin d'Afrique Noire*, **6805**, 269-278. http://www.santetropicale.com

[19] Davwar, P.M., Okeke, E., Duguru, M., Nyam, D., Bell, K., Odeghe, E.A., *et al*. (2023) Hepatocellular Carcinoma Presentation and Prognosis among Nigerian Adults with and without HIV. *PLOS ONE*, **18**, e0282539. https://doi.org/10.1371/journal.pone.0282539

[20] Diallo, I., Ndiaye, B., Touré, M., Sow, A., Mbengue, A., Diawara, P.S., *et al*. (2021) Hepatocellular Carcinoma in Senegal: Epidemiological, Clinical and Etiological Aspects about 229 Cases at Hospital Principal de Dakar. *Pan African Medical Journal*, **38**, Article 99. https://doi.org/10.11604/pamj.2021.38.99.25195

[21] Bekolo, N.W., Eloumou, B., Maïson, A., Ndjitoyap, N.A., Malongue, A. and Noah, N.D. (2024) Facteurs Pronostiques du Carcinome Hépatocellulaire au Cameroun: Une Étude Transversale. *Health Science and Disease*, **25**, 1-4.

[22] Kondé, A., Sidibé, L., Diarra, A., Fofana, Y., Samaké, D., Bah, M., *et al*. (2023) Epidemiological Aspects of Cirrhosis at the Sominé Dolo Hospital in Mopti. *SAS Journal of Surgery*, **9**, 438-441. https://doi.org/10.36347/sasjs.2023.v09i05.020

[23] Mahassadi, A.K., Anzouan-Kacou Kissi, H. and Attia, A.K. (2021) The Prognostic Values of Neutrophil-to-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio at Baseline in Predicting the In-Hospital Mortality in Black African Patients with Advanced Hepatocellular Carcinoma in Palliative Treatment: A Comparative Cohort Study. *Hepatic Medicine: Evidence and Research*, **13**, 123-134. https://doi.org/10.2147/hmer.s333980

[24] Mossanen, J.C. and Tacke, F. (2013) Role of Lymphocytes in Liver Cancer. *OncoImmunology*, **2**, e26468. https://doi.org/10.4161/onci.26468

[25] Tang, J., Yan, Z., Feng, Q., Yu, L. and Wang, H. (2021) The Roles of Neutrophils in the Pathogenesis of Liver Diseases. *Frontiers in Immunology*, **12**, Article 625472. https://doi.org/10.3389/fimmu.2021.625472

[26] Liao, K., Zhang, X., Liu, J., Teng, F., He, Y., Cheng, J., *et al*. (2023) The Role of Platelets in the Regulation of Tumor Growth and Metastasis: The Mechanisms and Targeted Therapy. *MedComm*, **4**, e350. https://doi.org/10.1002/mco2.350

[27] Rea, I.M., Gibson, D.S., McGilligan, V., McNerlan, S.E., Alexander, H.D. and Ross, O.A. (2018) Age and Age-Related Diseases: Role of Inflammation Triggers and Cytokines. *Frontiers in Immunology*, **9**, Article 586. https://doi.org/10.3389/fimmu.2018.00586

[28] Suner, A. and Carr, B.I. (2020) Platelet-to-Lymphocyte and Neutrophil-to-Lymphocyte Ratios Predict Tumor Size and Survival in HCC Patients: Retrospective Study. *Annals of Medicine and Surgery*, **58**, 167-171. https://doi.org/10.1016/j.amsu.2020.08.042

[29] Aldridge, D.R., Tranah, E.J. and Shawcross, D.L. (2015) Pathogenesis of Hepatic

Encephalopathy: Role of Ammonia and Systemic Inflammation. *Journal of Clinical and Experimental Hepatology*, **5**, S7-S20. https://doi.org/10.1016/j.jceh.2014.06.004

[30] Lin, S., Hu, S., Ran, Y. and Wu, F. (2021) Neutrophil-to-Lymphocyte Ratio Predicts Prognosis of Patients with Hepatocellular Carcinoma: A Systematic Review and Meta-analysis. *Translational Cancer Research*, **10**, 1667-1678. https://doi.org/10.21037/tcr-20-3237

[31] Ismael, M.N., Forde, J., Milla, E., Khan, W. and Cabrera, R. (2019) Utility of Inflammatory Markers in Predicting Hepatocellular Carcinoma Survival after Liver Transplantation. *BioMed Research International*, **2019**, Article ID: 7284040. https://doi.org/10.1155/2019/7284040

[32] Chen, T., Lin, C., Huang, P. and Wen, C. (2012) Neutrophil-to-Lymphocyte Ratio Associated with Mortality in Early Hepatocellular Carcinoma Patients after Radiofrequency Ablation. *Journal of Gastroenterology and Hepatology*, **27**, 553-561. https://doi.org/10.1111/j.1440-1746.2011.06910.x

Appendix 1: Standardized Survey Form

File number..... Year.....

Entry date..... Date of discharge.....

Epidemiological data

Age..... Sex..... Religion.....

Level of education..... Profession.....

Prognostic data

Neutrophiles……

Lymphocytes……

Platelet……..

Performance status score (WHO): 01/2/3/4

Edemato-ascitic decompensation/yes/no/

Abundance of ascites: absent or low/medium/high

Prothrombin rate..... Total bilirubin .....

conjugated bilirubin..... Glasgow score.....

Asterixis..... Jaundice.. /yes/no/

Hepatic encephalopathy: Absent grade I grade II grade IIIa grade IIIb

Child Pugh score: A/B/C; BCLC: A/B/C/D/

Ascites fluid infection/yes/no/. Digestive hemorrhage/yes/no/.

Liver size.....Number of nodule .....Nodule size.....

Portal vein thrombosis/yes/no/

Extrahepatic metastasis: peritoneal/pulmonary/bone/Other.....

Death: Yes/no

Lengh of stay…….