Prognostic Value of Neutrophil/Lymphocyte Ratio in Patients with Hepatocellular Carcinoma Treated with Transarterial Chemoembolization

Kevin C. McLean, Seoiyoung Ahn, Shelby K. Frantz, Olidapo R. Adeniran, Thomas Y. Wong, Jessica T. Wen, Jennifer M. Watchmaker, Hui Wu, Shawn P. Garbett, Jennifer Baker, Anthony J. Borgmann, David Duncan, Daniel B. Brown
Vanderbilt University Medical Center, Department of Radiology

Symposium on Clinical Interventional Oncology

Background

- Hepatocellular Carcinoma (HCC) represents the sixth leading cause of cancer and the third leading cause of cancer-related mortality with a 5-year survival rate of less than 20%.
- TACE has been reported to improve the survival of patients with surgically unresectable HCC. However, survival following TACE varies greatly, ranging from less than a year up to 47 months. Therefore, identifying the prognostic factors that would predict oncologic outcomes after TACE has become an area of interest.
- Prior studies have demonstrated that elevated baseline neutrophil/lymphocyte ratio (NLR) is associated with high rates of immediate HCC progression after TACE.
- Additional factors such as Child-Pugh (CP) score and Barcelona Clinic Liver Cancer (BCLC) staging have been utilized as prognostic factors to determine response to TACE.

Purpose

To evaluate predictors of overall survival in patients with hepatocellular carcinoma treated with lipiodol transarterial chemoembolizaton (cTACE).

Materials and Methods

- A total of 228 patients (75% male) with treatment naïve HCC were reviewed. All patients were treated exclusively with conventional TACE.
- Baseline labs included liver function tests and complete blood count with differential to calculate neutrophil/lymphocyte ratio (NLR).
- Overall survival (OS) and progression-free survival (PFS) were assessed using Chi-Squared, and Kaplan-Meier analysis.
- Cox Proportional Hazards (CPH) model was performed to gauge the effects of NLR, CP, BCLC, ALBI, age, sex, tumor number and etiology of cirrhosis on OS and PFS.

Table 1: Study Group Demographics: (A) Baseline patient demographics and etiology of cirrhosis. (B) Baseline lab values, baseline CP and BCLC stage

A

Patient #	228
Age (years)	64 (22-84)
Sex	
Male	164 (75%)
Female	54 (25%)
Hepatitis B	11 (5.0%)
Hepatitis C	110 (50%)
EtOH	66 (30%)
NASH	44 (20%)

B

ALBI Score 1	61 (27%)
ALBI Score 2	156 (69%)
ALBI Score 3	11 (4%)
Median total bilirubin	1.1
Median INR	1.2
Median Albumin	3.6
Median NLR	2.5
Child-Pugh (CP) A	153 (67%)
CP B-C	74 (33%)
Barcelona Clinic Liver Cancer (BCLC) Staging 0-A	134 (59%)
B	80 (35%)
C	14 (6%)

Results

Figure 1. Kaplan Meier Curves demonstrating: (A) OS and PFS for patients treated with cTACE. (B) OS for CP A and CP B/C. (C) OS for BCLC stage 0, A, B, and C. (D) OS for ALBI Grade 1, 2, and 3. (E) OS for NLR >/= 4 compared to NLR <4.

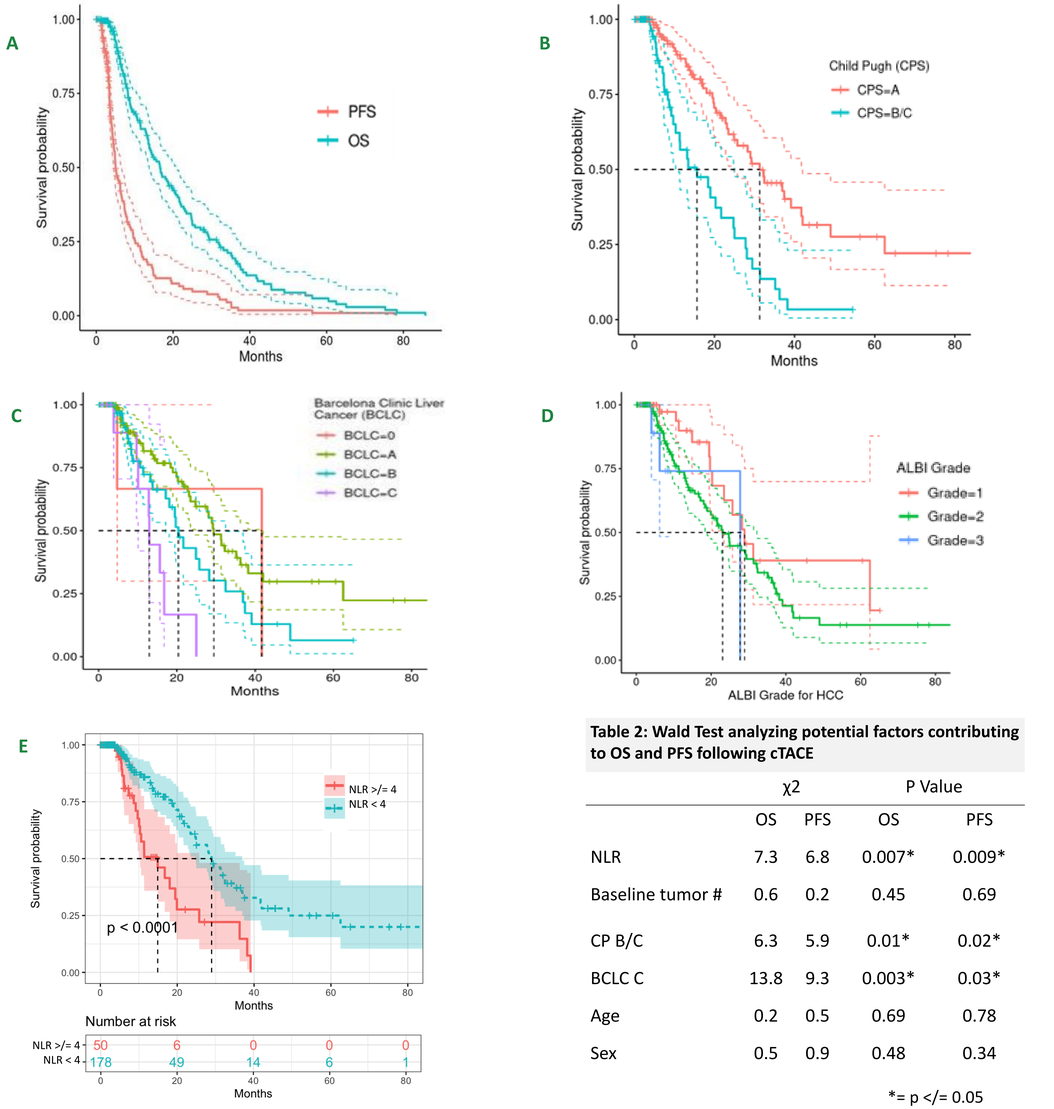

Table 2: Wald Test analyzing potential factors contributing to OS and PFS following cTACE

	χ2		P Value	
	OS	PFS	OS	PFS
NLR	7.3	6.8	0.007*	0.009*
Baseline tumor #	0.6	0.2	0.45	0.69
CP B/C	6.3	5.9	0.01*	0.02*
BCLC C	13.8	9.3	0.003*	0.03*
Age	0.2	0.5	0.69	0.78
Sex	0.5	0.9	0.48	0.34

*= p </= 0.05

Results Continued

- Median [95%CI] OS was 25 months [21.6-31.4]. Median PFS was 8.0 months [5.1-13.4].
- Median OS was longer for CP A (31.3 months [24.9-42]) compared to CP B/C patients (15.6 months [10.3-25]) (X2=23.1, p<0.0001). Median PFS was longer for CP A (12.2 months [7.8-NR]) than CP B patients (5.0 months [3.3-11.5]) (X2=9.5, p=0.002).
- Median OS was longer for BCLC 0/A patients (29.4 months [24.7-41.7]) than BCLC B (20.4 months [17.2-32.4]) and BCLC C (12.9 months [10.1-NR]) (X2=15.2, p<0.0001). PFS was longer for BCLC 0/A patients (11.8 months [8.0-NR]) than BCLC B (5.1 months [3.8-NR]) and BCLC C (3.6 months [3.2-NR]) (X2=11.6, p=0.003).
- Median OS was not different for ALBI 1 (28.9 months [23.5-NR]) and ALBI 2 patients (23 months [19-32.2]) (p=0.08). ALBI was not predictive of PFS (p>0.05).
- Median NLR in patient with immediate disease progression following cTACE was 4.19. Patients with baseline NLR >/= 4 had a significantly higher rate of progressive disease following cTACE compared to those with baseline NLR < 4 (χ2= 17.3, p < 0.0001).
- Median OS was longer for patients with NLR < 4 (28.9 months [24.7-36.9]) compared to patients with NLR >/= 4 (14.9 months [10.1-25.7]).
- In CPH model, NLR (HR: 7.3, p=0.007), CP B score (HR: 6.3, p=0.01), and BCLC C score (HR: 13.8, p=0.003) predicted worse outcomes for OS.
- For PFS, baseline NLR (HR: 6.8, p=0.009), CP B Score (HR: 5.9, p=0.02) and BCLC C score (HR 9.3, p=0.03) predicted worse outcomes.
- The other factors were not predictive.

Discussion

- Given the variability in response to TACE in patients with HCC, studies have sought to identify factors which may aid in predicting outcomes and allow a more tailored treatment strategy.
- NLR is widely used as a biomarker for immune response to various infectious and non-infectious stimuli and is being investigated as a biomarker for many different tumors including HCC.
- This study demonstrates the predictive value of baseline NLR in determining survival outcomes in patients with HCC treated with cTACE.

Conclusion

- cTACE resulted in a median OS of 25 months for the whole cohort and 31 months for CP A patients. In addition to advanced CP and BCLC scores, a higher baseline NLR predicted shorter OS and PFS following cTACE.

Acknowledgements

This study was supported by Guerbet.