

ORIGINAL ARTICLE

Prognostic significance of neutrophil to lymphocyte ratio in patients with gallbladder carcinoma

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Abstract

Background: Numerous literature suggest that the preoperative neutrophil to lymphocyte ratio (NLR) is correlated to the prognosis of various cancers. However, the prognostic significance of NLR in gallbladder carcinoma (GBC) remains to be determined.

Methods: Data from 316 GBC patients with surgical treatment were reviewed retrospectively. A receiver operating characteristic (ROC) curve was performed to determine an optimal cut-off value for NLR. The Kaplan–Meier method and Cox regression proportional hazard model were performed to evaluate prognostic factors.

Results: The optimal cut-off point for NLR was 2.61 according to the ROC curve. According to the univariable analysis, NLR, differentiation and TNM stage were associated with GBC prognosis. GBC patients with NLR > 2.61 have worsened 5-year overall survival (OS) compared to patients with NLR ≤ 2.61 (P < 0.001). Multiple analyses indicated that NLR (hazard ratio (HR) 1.65; 95 percent confidence interval (95% CI) 1.25–2.17), differentiation (HR 1.25; 95% CI 0.97–1.62) and TNM stage (HR 3.79; 95% CI 2.09–6.87) were independent prognostic factors for GBC. GBC patients in stage III/IV, NLR > 2.61 exhibited worse OS compared to patients with NLR ≤ 2.61 (P < 0.05). A prognostic evaluation model based on the independent prognostic factors was established.

Conclusion: NLR is associated with GBC prognosis and is a potential prognostic marker for GBC, not only preoperatively but also postoperatively.

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Introduction

Gallbladder carcinoma (GBC) is relatively rare worldwide but is the most prevalent cancer in the biliary tract system.¹ In recent years, this fatal disease has attracted more and more public attention due to patients' poor prognosis. According to epidemiological studies, the 5-year overall survival (OS) for GBC patients is less than 10%,^{2,3} which could be attributed to nonspecific

symptoms, late diagnosis, lack of treatment options, and absence of effective prognostic markers. If an ideal marker existed to identify patients with poor prognosis, aggressive measures could be adopted, and the OS of GBC patients could improve.

Previous studies demonstrated that inflammation was involved in the genesis and progression of tumors.^{4,5} The presence of neutrophils and lymphocytes in the peripheral blood is representative of a systemic inflammation response. The neutrophil to lymphocyte ratio (NLR) has been investigated as a potential prognostic marker in a variety of cancers. Azab *et al.*⁶

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revealed that NLR was a useful predictor in short- and long-term mortality of breast cancer patients. Stotz *et al.*⁷ have investigated prognostic implications of NLR in patients with primary operable and inoperable pancreatic cancer and concluded that increased NLR indicated a poor prognosis regardless of therapeutic modality. Sharaiha *et al.*⁸ confirmed that NLR was a potential prognostic marker for recurrence and death after

esophagectomy. In addition, similar findings were observed in gastric cancer,⁸ hepatocellular carcinoma,⁹ colorectal cancer,¹⁰ lung cancer^{11,12} and renal cancer.¹³ Elevated NLR is therefore implicated in poor prognosis of patients with malignancy.

GBC is proposed to be an inflammation-related malignancy.¹⁴ Cholecystitis is a recognized risk factor present in a majority of GBC patients. Some researchers noted that the interaction between cholecystitis and gallstones promoted malignant transformation of gallbladder epithelial cells. Han *et al.*¹⁵ found that inflammation can influence GBC prognosis. Based on the fact that NLR is an effective prognostic indicator in other cancers, NLR may have a similar role in GBC. However, reports about the association between NLR and GBC prognosis were rare.

Therefore, the present study aims to clarify the relationship between NLR and GBC prognosis and to explore an effective prognostic marker for this malignancy.

Table 1 Clinic-pathological characteristics of 316 patients with GBC

| Items | Cases (N, %) | Mean \pm SD |
|---|--------------|--------------------|
| Age (years) | | 63.51 \pm 10.99 |
| >55 | 238 (75.32) | – |
| \leq 55 | 78 (24.68) | – |
| Gender | | |
| Male | 101 (31.96) | – |
| Female | 215 (68.04) | – |
| Blood type | | |
| A | 80 (25.32) | – |
| B | 118 (37.34) | – |
| AB | 42 (13.29) | – |
| O | 76 (24.05) | – |
| Gallstones | | |
| Present | 160 (50.63) | – |
| Absent | 156 (49.37) | – |
| Differentiation | | |
| High | 26 (8.23) | – |
| Moderate | 134 (42.41) | – |
| Low | 156 (49.36) | – |
| Tumor stage | | |
| I/II | 28 (9.18) | – |
| III/IV | 288 (90.82) | – |
| pT category | | |
| T1/T2 | 53 (16.77) | – |
| T3/T4 | 263 (83.23) | – |
| pN category | | |
| N0 | 161 (50.95) | – |
| N1 | 155 (49.05) | – |
| pM category | | |
| M0 | 231 (73.10) | – |
| M1 | 85 (26.90) | – |
| Neutrophil cell count ($\times 10^9/L$) | – | 4.95 \pm 3.05 |
| Lymphocyte cell count ($\times 10^9/L$) | – | 1.28 \pm 0.54 |
| Neutrophil to lymphocyte ratio | – | 5.11 \pm 6.23 |
| Red blood cell count ($\times 10^9/L$) | – | 3.88 \pm 0.61 |
| Platelet count ($\times 10^9/L$) | – | 196.37 \pm 85.36 |
| White blood cell ($\times 10^9/L$) | – | 6.89 \pm 3.36 |

GBC: gallbladder carcinoma; Tumor stage: according to the American Joint Committee on Cancer (the 6th edition).

Materials and methods

Patients

Data from 316 GBC patients after surgery at the First Affiliated Hospital of Medical College, Xi'an Jiaotong University between January 2002 and January 2013 were reviewed retrospectively. All final diagnoses were confirmed by pathologic examination. Patients with no documented preoperative lymphocyte and

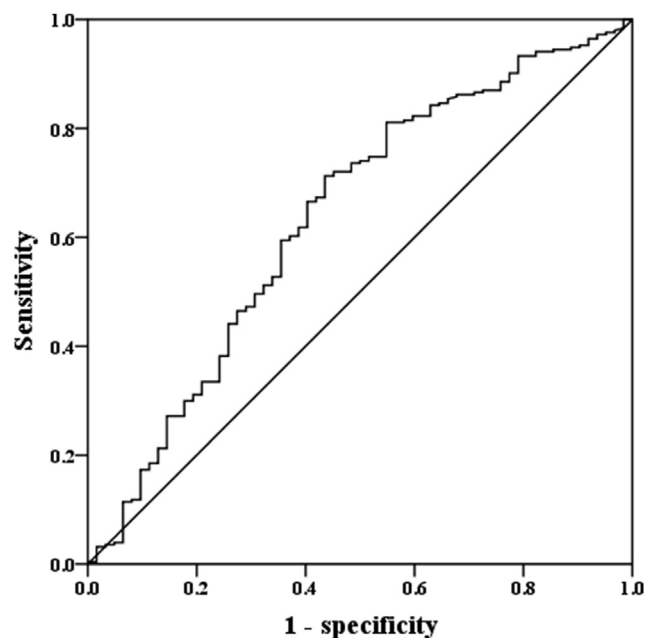


Figure 1 A ROC curve to identify the optimal cut-off value of NLR. The area under the curve was 0.637 (95% confidence interval: 0.556–0.718). The appropriate cut-off point for NLR was 2.61 with the highest sum of a sensitivity (71.3%) and a specificity (56.5%). ROC: receiver operating characteristic; NLR: neutrophil to lymphocyte ratio; GBC: primary gallbladder carcinoma

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