# Prognostic Role of Preoperative Direct Bilirubin-to-Indirect Bilirubin Ratio and Neutrophils -to-Lymphocytes in Resectable Colorectal Cancer

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## BACKGROYND

Many clinical studies have shown that bilirubin level may predict prognosis of colorectal cancer (CRC). Neutrophils-to-lymphocytes (NLR) is a well-known prognostic factor for colorectal cancer with high predictive performance. The aim of our study was to combine the two to find a highly specific and potent prognostic factor for resectable colorectal cancer.

## METHODS

Our study included 702 patients histopathologically confirmed CRC who had undergone resection of primary lesions at Hubei Cancer Hospital. Routine preoperative serum biochemical examinations were performed within one week before surgery. The DIR was defined as the level of direct bilirubin divided by the level of indirect bilirubin. Patients were divided into a high-level group or a low-level group according to the cut-off values of the DIR and NLR level. Patients with a low DIR and low NLR level were scored as 0, those with a high DIR or a high NLR level were scored as 1, and those with a high DIR and high NLR level were scored as 2. The entire population was randomly assigned to a training (491) or validation (211) group. Chi-square tests, Kaplan-Meier survival analyses, and univariate and multivariate Cox regression analyses were used to evaluate prognosis. The accuracy of the model was evaluated by Harrell's concordance index (C-index) and the Brier score.
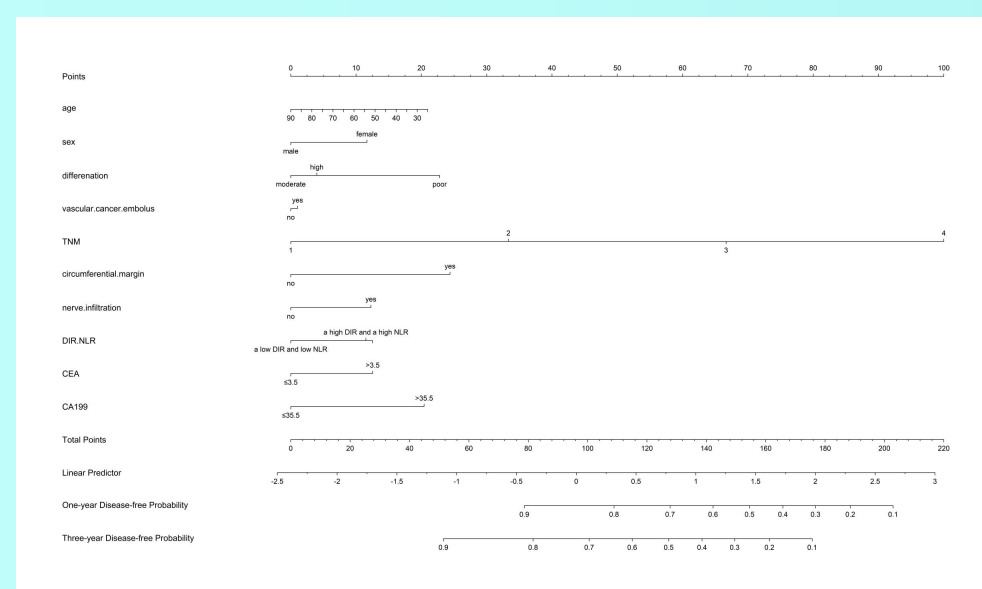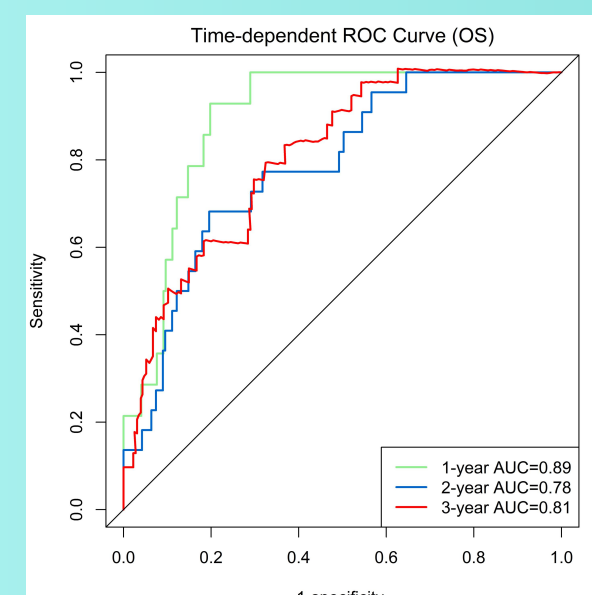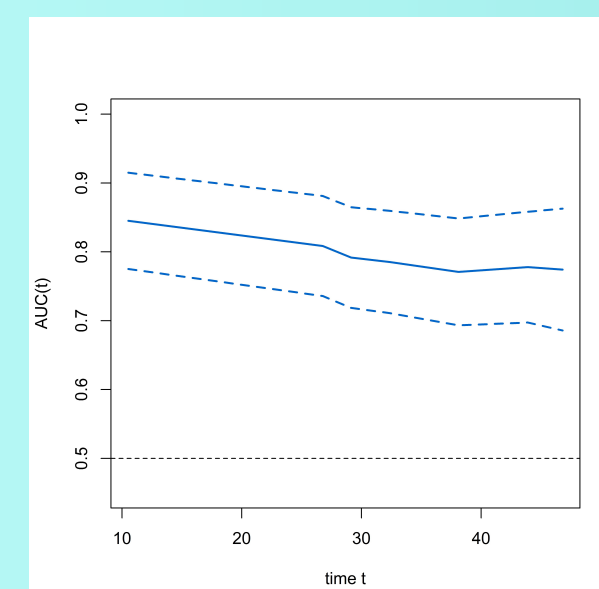
## RESULTS  and  CONCLUSIONS
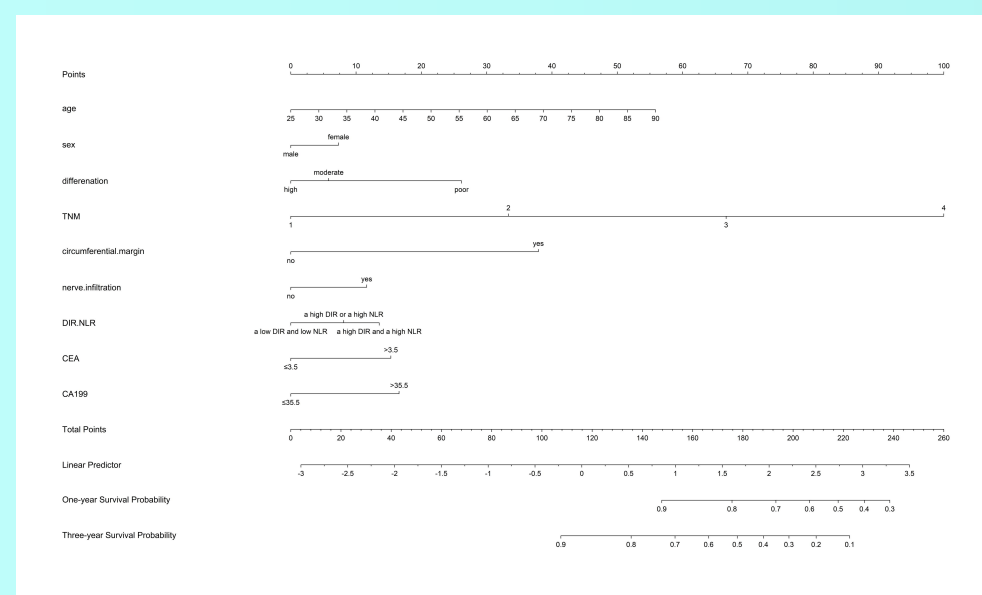


Nomogram of prognostic model for OS of colorectal cancer



Nomogram of prognostic model for DFS of colorectal cancer
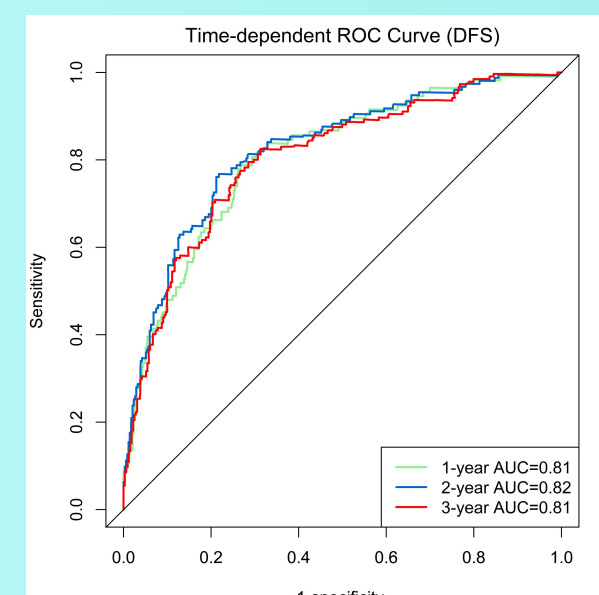


ROC curves for the OS and DFS



Time-AUC curves from the nomograms for the prediction of OS and DFS rates

The median follow-up time was 35 months. Besides, the combination of DIR and NLR (DIR-NLR) was an independent prognostic factor in dieases-free survival (DFS) for patients with resectable CRC (HR: 1.323; 95% CI, 1.072-1.633). More interestingly, the prognostic model based on age, sex, TNM stage, differenation, circumferential margin, vascular cancer embolus status, nerve infiltration status, DIR-NLR, CEA and CA199 was found to present exceptional performance in overall survival (OS) prediction [C-index: 0.782 (95% CI, 0.73-0.83) and Brier score: 0.035 for 1-year OS and 0.072 for 3-year OS]. Moreover, the prognostic model also was found to present exceptional performance in DFS prediction [C-index: 0.769 (95% CI, 0.73-0.80) and Brier score: 0.078 for 1-year OS and 0.124 for 3-year OS].
We successfully established a novel biomarker based on bilirubin and NLR to guide clinical decision-making for CRC.