Heliyon 9 (2023) e21772

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Assessment of the albumin-bilirubin score in breast cancer patients with liver metastasis after surgery☆

Li Chen [a,b,1], Chunlei Tan [c,1], Qingwen Li [d,1], Zhibo Ma [d,1], Meng Wu [d], Xiaosheng Tan [d,****], Tiangen Wu [e,***], Jinwen Liu [a,**], Jing Wang [b,*]

[a] Department of Thyroid and Breast Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, 430030, PR China

[b] Department of Breast Surgical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100021, PR China

[c] Department of Breast Surgery, Harbin Medical University Cancer Hospital, Harbin, Heilongjiang, 150081, PR China

[d] Institute of Organ Transplantation, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Key Laboratory of Organ Transplantation, Ministry of Education, NHC Key Laboratory of Organ Transplantation, Chinese Academy of Medical Sciences, Wuhan, Hubei 430030, PR China

[e] Department of Hepatobiliary&Pancreatic Surgery, Zhongnan Hospital of Wuhan University,Wuhan, Hubei, 430071, PR China

ARTICLE INFO

Keywords:
Breast cancer
Albumin-bilirubin grade
Albumin
Bilirubin
Liver metastasis

ABSTRACT

Objective: This study aims to investigate the potential prognostic value of albumin-bilirubin (ALBI) score in breast cancer patients with liver metastasis after surgery.

Methods: This was a retrospective study of 178 breast cancer patients with liver metastasis after surgery. ALBI score was calculated by the following formula: (log10 bilirubin × 0.66) − (albumin × 0.085). The optimal cutoff value of ALBI score was assessed by X-tile. The clinical influence of ALBI score on survival outcomes using Kaplan-Meier method, Log-rank test, Cox proportional hazards regression model. The calibration curves, decision curve analysis and time-dependent ROC curve were used to assess the predictive performance of the nomogram's models.

Results: The classifications of 178 breast cancer patients with liver metastasis after surgery were as follows: low ALBI score group (< −3.36) vs. high ALBI score group (≥−3.36). The Cox proportional hazards regression model indicated that ALBI score was a potential predictor. Kaplan-Meier survival curve performed that the median disease free survival (p = 0.0029) and overall survival

☆ Institutional Review Board Statement.

* Corresponding authors. Department of Breast Surgical Oncology, National Cancer Center/National Clinical Research Center for Cancer/Cancer Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, 100021, PR China.

** Corresponding author. Department of Thyroid and Breast Surgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, Hubei, 430030, PR China.

*** Corresponding authors. Department of Hepatobiliary&Pancreatic Surgery, Zhongnan Hospital of Wuhan University,Wuhan, Hubei, 430071, PR China.

**** Corresponding author. Institute of Organ Transplantation, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Key Laboratory of Organ Transplantation, Ministry of Education, NHC Key Laboratory of Organ Transplantation, Chinese Academy of Medical Sciences, Wuhan, Hubei 430030, PR China.

E-mail addresses: txs900416@163.com (X. Tan), wtg666@whu.edu.cn (T. Wu), Liujinwen@tjh.tjmu.edu.cn (J. Liu), wangjing@cicams.ac.cn (J. Wang).

[1] These authors contributed equally to this article.

https://doi.org/10.1016/j.heliyon.2023.e21772
Received 13 September 2023; Received in revised form 25 October 2023; Accepted 27 October 2023
Available online 30 October 2023

(p < 0.0001) in low ALBI score group were longer than in high ALBI score group. The ALBI-based nomograms had good predictive performance.
Conclusions: The ALBI score has high prognostic ability for survival time in breast cancer with liver metastasis after surgery. These models will be valuable in discriminating patients at high risks of liver metastasis.

1. Introduction

Breast cancer is an onerous public health burden and the leading cause of cancer-related deaths in females all over the world [1]. There is a wide variety of therapeutic options for patients with breast cancer, according to Tumor-Node-Metastasis (TNM) staging system and performance status [2]. Surgical operation is the unique potential therapeutic method. Unfortunately, more than half of breast cancer deaths are caused by distant metastasis [3]. Take into consideration of the high incidence rate and aggressive behavior, patients diagnosed with breast cancer need to be classified to comply with the severity of the disease. And this classification can direct patients to select the appropriate treatment method. In clinical practice, it is distinguished to employ the markers that are prone to measure by non-invasive techniques. Serum tumor markers are quite prone to determine, together with beneficial for diagnosis and prediction of survival. Currently, prognostic factors such as carbohydrate antigen 125 (CA125), carbohydrate antigen 15–3 (CA15-3), carcinoembryonic antigen (CEA) have been proposed to this aim [4–6]. However, these tumor markers can be found normal in a small portion of breast cancer patients. Hence, more sensitive and efficient markers are required to predict the prognosis of breast cancer patients.

In recent years, there has been increasing interest in creating predictive biomarkers for plethora cancers based on serological and hematological tests. Johnson PJ and colleagues reported the albumin-bilirubin (ALBI) grade, which was based on serum bilirubin and albumin levels, acted as a novel model for objective measure of liver function [7]. The ALBI grade was initially applied to evaluate the severity of liver dysfunction in liver cancer patients. Some studies have proved that ALBI grade could predict the prognosis in hepatocellular carcinoma patients with resectable, recurrence or locally advanced disease [8–10]. Moreover, recent studies have also indicated that ALBI grade had prognostic value in a plethora of cancers including non-small-cell lung cancer, pancreatic cancer, intrahepatic cholangiocarcinoma, advanced gastric cancer, colorectal cancer [11–15]. The breast cancer commonly proliferates to liver, lungs, brain and bone. The survival time of breast cancer patients with liver metastasis without treatment is usually less than 9 months [16]. To our knowledge, there is currently no research in the literature to demonstrate the practicality of ALBI grade in predicting the prognosis of breast cancer with liver metastasis after surgery. Therefore, we aim to explore the prognostic value of ALBI grade in breast cancer patients with liver metastasis after surgery.

2. Methods

2.1. Ethics approval and consent to participate

This retrospective single center study was conducted in accordance with the amended Declaration of Helsinki, and was approved by the ethics committee of Cancer Hospital Chinese Academy of Medical Sciences (Approved no.82173328). The enrolled patients provided written informed consent for using their data in this retrospective study. The individual patient information has been protected.

2.2. Patients and samples enrolled in this study

From our database, we retrospectively identified 178 breast cancer with liver metastasis after surgery. These patients were treated and followed up from 2000 through 2018 at Cancer Hospital Chinese Academy of Medical Sciences. We groped the clinical and pathological data according to the electronic medical records.

2.3. Inclusion criteria and exclusion criteria

Inclusion requirements were that: 1) breast cancer patients with liver metastasis after surgery when followed up; 2) medical records with complete data and follow-up information. Exclusion requirements were that: 1) breast cancer patients with multiple metastases, such as lungs, brain and bone; 2) missing data and lost to follow up.

2.4. Calculation of albumin-bilirubin (ALBI) score

The albumin-bilirubin (ALBI) score was an indicator that combined the albumin and direct bilirubin level. Serum albumin and direct bilirubin were detected centrally at study baseline in this research. ALBI score was calculated based on the following formula: (log10 bilirubin $\times$ 0.66) $-$ (albumin $\times$ 0.085), where bilirubin was in μmol/L and albumin in g/L. The optimal cutoff value of ALBI score was assessed by X-tile. In this study, patients were then grouped into two categories based on the ALBI score as low ALBI score group (< -3.36) vs. high ALBI score group ($\geq$-3.36).

Table 1
Clinical characteristics of the breast cancer patients with liver metastasis after surgery according to ALBI score.

Characteristic	level	Low ALBI	High ALBI	p
n		129	49	
Age	< 49	75 (58.1)	23 (46.9)	0.241
	≥49	54 (41.9)	26 (53.1)	
Marital status	Married	125 (96.9)	49 (100.0)	0.496#
	Unmarried	4 (3.1)	0 (0.0)	
BMI	< 23.51	65 (50.4)	24 (49.0)	1.000
	≥23.51	64 (49.6)	25 (51.0)	
Family history	No	106 (82.2)	34 (69.4)	0.098
	Yes	23 (17.8)	15 (30.6)	
Menarche age	< 14	36 (27.9)	14 (28.6)	1.000
	≥14	93 (72.1)	35 (71.4)	
Menopause	No	85 (65.9)	20 (40.8)	0.004
	Yes	44 (34.1)	29 (59.2)	
ABO blood type	A	27 (20.9)	9 (18.4)	0.632#
	B	45 (34.9)	20 (40.8)	
	O	45 (34.9)	18 (36.7)	
	AB	12 (9.3)	2 (4.1)	
Type of surgery	Mastectomy	120 (93.0)	49 (100.0)	0.130#
	Breast-conserving surgery	9 (7.0)	0 (0.0)	
Pathological tumor size	≤2 cm	45 (34.9)	15 (30.6)	0.394#
	> 2 and ≤5 cm	69 (53.5)	31 (63.3)	
	> 5 cm	15 (11.6)	3 (6.1)	
Histologic grade	I	5 (3.9)	6 (12.2)	0.043
	II	74 (57.4)	31 (63.3)	
	III	50 (38.8)	12 (24.5)	
Pathological T stage	T1	37 (28.7)	11 (22.4)	0.620#
	T2	72 (55.8)	32 (65.3)	
	T3	10 (7.8)	2 (4.1)	
	T4	10 (7.8)	4 (8.2)	
Pathological N stage	N0	26 (20.2)	7 (14.3)	0.228
	N1	29 (22.5)	7 (14.3)	
	N2	38 (29.5)	14 (28.6)	
	N3	36 (27.9)	21 (42.9)	
Pathological TNM stage	I	6 (4.7)	5 (10.2)	0.060
	II	45 (34.9)	9 (18.4)	
	III	78 (60.5)	35 (71.4)	
Total lymph nodes (TLN)	< 19	63 (48.8)	23 (46.9)	0.953
	≥19	66 (51.2)	26 (53.1)	
Positive lymph nodes (PLN)	< 5	69 (53.5)	17 (34.7)	0.038
	≥5	60 (46.5)	32 (65.3)	
Molecular subtype	Luminal A	3 (2.3)	7 (14.3)	0.002#
	Luminal B HER2+	18 (14.0)	13 (26.5)	
	Luminal B HER2-	64 (49.6)	13 (26.5)	
	HER2 enriched	24 (18.6)	9 (18.4)	
	Triple negative	20 (15.5)	7 (14.3)	
ER	Negative	43 (33.3)	17 (34.7)	1.000
	Positive	86 (66.7)	32 (65.3)	
PR	Negative	45 (34.9)	15 (30.6)	0.718
	Positive	84 (65.1)	34 (69.4)	
HER2	Negative	86 (66.7)	27 (55.1)	0.209
	Positive	43 (33.3)	22 (44.9)	
Ki67	Negative	38 (29.5)	20 (40.8)	0.206
	Positive	91 (70.5)	29 (59.2)	
AR	Negative	124 (96.1)	48 (98.0)	0.888#
	Positive	5 (3.9)	1 (2.0)	
CK5/6	Negative	113 (87.6)	43 (87.8)	1.000
	Positive	16 (12.4)	6 (12.2)	
E-cad	Negative	71 (55.0)	27 (55.1)	1.000
	Positive	58 (45.0)	22 (44.9)	
EGFR	Negative	118 (91.5)	44 (89.8)	0.955
	Positive	11 (8.5)	5 (10.2)	
P53	Negative	73 (56.6)	26 (53.1)	0.799
	Positive	56 (43.4)	23 (46.9)	
TOP2A	Negative	91 (70.5)	34 (69.4)	1.000
	Positive	38 (29.5)	15 (30.6)	
Lymph vessel invasion	Negative	82 (63.6)	36 (73.5)	0.284
	Positive	47 (36.4)	13 (26.5)	
Neural invasion	Negative	118 (91.5)	45 (91.8)	1.000#

(*continued on next page*)

Table 1 (*continued*)

Characteristic	level	Low ALBI	High ALBI	p
n		129	49	
	Positive	11 (8.5)	4 (8.2)	
Postoperative chemotherapy	No	28 (21.7)	13 (26.5)	0.629
	Yes	101 (78.3)	36 (73.5)	
Postoperative radiotherapy	No	34 (26.4)	13 (26.5)	1.000
	Yes	95 (73.6)	36 (73.5)	
Postoperative endocrine therapy	No	46 (35.7)	23 (46.9)	0.227
	Yes	83 (64.3)	26 (53.1)	
Postoperative targeted therapy	No	100 (77.5)	40 (81.6)	0.694
	Yes	29 (22.5)	9 (18.4)	

Abbreviation: BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, Human Epidermal Growth Factor Receptor 2; AR, androgen receptor; CK5/6, Cytokeratin 5/6; E-cad, E-cadherin; EGFR, Epidermal Growth Factor Receptor; TOP2A, topoisomerase 2A.
[#]Fisher's exact test.

2.5. Follow-up

All patients had routine checkups with a physical examination, hematology examination, breast ultrasound, or CT every three months. Disease free survival (DFS) was defined as the time from surgery to progression with live metastasis. Overall survival (OS) was defined as the time from surgery to the date of death from any cause or last follow-up.

2.6. Statistical analysis

All statistical analyses were performed using the IBM SPSS Statistics (version 23.0; SPSS Inc., Chicago, IL, USA), GraphPad Prism software (version 8.0; GraphPad Inc., La Jolla, CA, USA), and R (version 4.2.2; Vienna, Austria. URL: http://www.R-project.org/). Categorical variables were presented as absolute values and percentages (%). The comparison of the rates between the groups were analyzed with Chi-square test or Fisher's exact test. The optimal cut-off value was calculated by X-tile. Survival analyses were performed using Kaplan-Meier method and Log-rank test. The potential factors were examined with Cox proportional hazards regression model analysis. Nomograms of the potential prognostic factors by the multivariate analysis for survival time were established with R software. The prediction accuracy was performed by time-dependent ROC curve, and area under the curve (AUC) for different survival time. The calibration curve and decision curve analysis (DCA) were generated comparing the observed results with the predicted results to assess the accuracy of predictive performance. A P-value of < 0.05 indicated statistical significance.

3. Results

3.1. Clinical characteristics of the patients enrolled in this study

Of 178 breast cancer patients with liver metastasis after surgery, all patients were female, with a median age of 49 years (range: 21–78 years). According to the optimal cut-off value of ALBI score by X-tile, patients with low ALBI score were 129 cases, and patients with high ALBI score were 49 cases. Table 1 summarized the clinical and pathological data of the 178 breast cancer patients with liver metastasis enrolled in this study. We explored the relationship between ALBI score and clinicopathological data, and found that ALBI score was significantly associated with menopause ($p = 0.004$), histologic grade ($p = 0.043$), positive lymph nodes ($p = 0.038$), molecular subtype ($p = 0.002$).

3.2. Comparison of serological and hematological characteristics by ALBI score

The common serological and hematological makers were detected in breast cancer patients with liver metastasis after surgery. In this study, we choose the median value as the grouping criterion. The serological and hematological characteristics of patients by ALBI score were summarized in Table 2. ALBI score was significantly associated with albumin(ALB) ($p < 0.001$), cholesterol(CHOL) ($p = 0.019$), total protein(TP) ($p = 0.005$).

4. The potential prognostic factors for DFS and OS

The prognostic factors for DFS according to the univariate and multivariate Cox proportional hazards regression model analyses were listed in Table 3. A multivariate analysis indicated that ALBI, Lactic dehydrogenase (LDH), Topoisomerase 2A (TOP2A) were the potential prognostic factors for DFS. The prognostic factors for OS based on the univariate and multivariate Cox proportional hazards regression model analyses were listed in Table 4. The multivariate analysis shown that ALBI, LDH, monocyte, ER, TOP2A were the potential prognostic factors for OS.

Table 2
Comparison of serological and hematological characteristics based on ALBI score in breast cancer patients with liver metastasis after surgery.

Characteristic	level	Low ALBI	High ALBI	p
n		129	49	
Alanine aminotransferase (ALT) (U/L)	< 17	61 (47.3)	26 (53.1)	0.603
	≥17	68 (52.7)	23 (46.9)	
Aspartate aminotransferase (AST) (U/L)	< 20	61 (47.3)	27 (55.1)	0.445
	≥20	68 (52.7)	22 (44.9)	
Lactic dehydrogenase (LDH) (U/L)	< 166	60 (46.5)	23 (46.9)	1.000
	≥166	69 (53.5)	26 (53.1)	
γ-glutamyl transpeptidase (γ-GT) (U/L)	< 17	53 (41.1)	27 (55.1)	0.131
	≥17	76 (58.9)	22 (44.9)	
Albumin (ALB) (g/L)	< 44.1	41 (31.8)	42 (85.7)	< 0.001
	≥44.1	88 (68.2)	7 (14.3)	
Total bilirubin (TBIL) (μmol/L)	< 8.60	66 (51.2)	21 (42.9)	0.411
	≥8.60	63 (48.8)	28 (57.1)	
Direct bilirubin (DBIL) (μmol/L)	< 2.75	70 (54.3)	19 (38.8)	0.093
	≥2.75	59 (45.7)	30 (61.2)	
Indirect bilirubin (IBIL) (μmol/L)	< 5.85	68 (52.7)	21 (42.9)	0.314
	≥5.85	61 (47.3)	28 (57.1)	
Cholesterol (CHOL) (mmol/L)	< 3.80	72 (55.8)	17 (34.7)	0.019
	≥3.80	57 (44.2)	32 (65.3)	
Triglyceride (TG) (mmol/L)	< 1.16	59 (45.7)	28 (57.1)	0.233
	≥1.16	70 (54.3)	21 (42.9)	
Total protein (TP) (g/L)	< 73.0	55 (42.6)	33 (67.3)	0.005
	≥73.0	74 (57.4)	16 (32.7)	
Globulin(G) (g/L)	< 29.0	62 (48.1)	25 (51.0)	0.853
	≥29.0	67 (51.9)	24 (49.0)	
Albumin/Globulin (A/G)	< 1.55	60 (46.5)	28 (57.1)	0.272
	≥1.55	69 (53.5)	21 (42.9)	
Prealbumin (PAB) (mg/dl)	< 27.0	63 (48.8)	22 (44.9)	0.763
	≥27.0	66 (51.2)	27 (55.1)	
Carbohydrate antigen 125 (CA125) (U/ml)	< 10.57	60 (46.5)	29 (59.2)	0.179
	≥10.57	69 (53.5)	20 (40.8)	
Carbohydrate antigen 153 (CA153) (U/ml)	< 13.01	64 (49.6)	25 (51.0)	1.000
	≥13.01	65 (50.4)	24 (49.0)	
Carcinoembryonic antigen (CEA) (ng/ml)	< 1.95	65 (50.4)	24 (49.0)	1.000
	≥1.95	64 (49.6)	25 (51.0)	
D-Dimer (DD) (mg/L)	< 0.21	67 (51.9)	21 (42.9)	0.360
	≥0.21	62 (48.1)	28 (57.1)	
Fibrinogen (FIB) (g/L)	< 2.75	64 (49.6)	25 (51.0)	1.000
	≥2.75	65 (50.4)	24 (49.0)	
ABO blood type	A	27 (20.9)	9 (18.4)	0.632[a]
	B	45 (34.9)	20 (40.8)	
	O	45 (34.9)	18 (36.7)	
	AB	12 (9.3)	2 (4.1)	
White blood cell ($\times 10^9$/L)	< 5.45	64 (49.6)	25 (51.0)	1.000
	≥5.45	65 (50.4)	24 (49.0)	
Neutrophils ($\times 10^9$/L)	< 3.23	65 (50.4)	23 (46.9)	0.808
	≥3.23	64 (49.6)	26 (53.1)	
Lymphocyte ($\times 10^9$/L)	< 1.70	67 (51.9)	21 (42.9)	0.360
	≥1.70	62 (48.1)	28 (57.1)	
Monocyte ($\times 10^9$/L)	< 0.35	65 (50.4)	24 (49.0)	1.000
	≥0.35	64 (49.6)	25 (51.0)	
Platelet ($\times 10^9$/L)	< 233	62 (48.1)	27 (55.1)	0.502
	≥233	67 (51.9)	22 (44.9)	

[a] Fisher's exact test.

4.1. Clinical impact of the ALBI grade on survival

Firstly, we explored the effects of the ALBI score on survival. Through the optimal cut-off value of ALBI score, 129 cases were in low ALBI score group, and 49 cases were in high ALBI score group. According to the ALBI score, median DFS was 45.80 months in low ALBI score group, 29.17 months in high ALBI score group (Log rank: $p = 0.0029$); median OS was 103.80 months in low ALBI score group, 55.77 months in high ALBI score group (Log rank: $p < 0.0001$) (Fig. 1A and B). According to the DFS, 1-year survival rate was 0.889 (95%CI, 0.835–0.945), 3-year survival rate was 0.560 (95%CI, 0.475–0.660), 5-year survival rate was 0.416 (95%CI, 0.326–0.530), 10-year survival rate was 0.181 (95%CI, 0.093–0.355), 15-year survival rate was 0.136 (95%CI, 0.057–0.328) in low ALBI score group; and 1-year survival rate was 0.809 (95%CI, 0.703–0.930), 3-year survival rate was 0.458 (95%CI, 0.330–0.634), 5-year survival rate was 0.206 (95%CI, 0.109–0.387), 10-year survival rate was 0.059 (95%CI, 0.011–0.307) in high ALBI score group. According to the OS, 1-year survival rate was 0.992 (95%CI, 0.977–1.000), 3-year survival rate was 0.836 (95%CI, 0.774–0.903), 5-year survival rate

Table 3
Univariate and multivariate survival analysis of disease free survival in breast cancer patients with liver metastasis after surgery.

Characteristics	Group	Univariate		95%CI		Multivariate		95%CI	
		P	HR	Low	High	P	HR	Low	High
ALBI	Low	1(Ref.)				1(Ref.)			
	High	0.028	2.601	1.109	6.101	0.000	2.637	1.709	4.067
Age	< 49	1(Ref.)							
	≥49	0.233	1.260	0.862	1.843				
Marital status	Married	1(Ref.)							
	Unmarried	0.137	5.088	0.598	43.311				
BMI	< 23.51	1(Ref.)							
	≥23.51	0.704	1.139	0.583	2.222				
Family history	No	1(Ref.)							
	Yes	0.623	1.182	0.606	2.306				
Menarche age	< 14	1(Ref.)							
	≥14	0.164	0.583	0.272	1.247				
Menopause	No	1(Ref.)							
	Yes	0.661	1.091	0.739	1.609				
Alanine aminotransferase (ALT)	< 17	1(Ref.)							
	≥17	0.890	0.944	0.414	2.153				
Aspartate aminotransferase (AST)	< 20	1(Ref.)							
	≥20	0.549	1.305	0.547	3.111				
Lactic dehydrogenase (LDH)	< 166	1(Ref.)				1(Ref.)			
	≥166	0.041	2.081	1.029	4.205	0.005	1.864	1.204	2.887
γ-glutamyl transpeptidase (γ-GT)	< 17	1(Ref.)							
	≥17	0.413	0.755	0.385	1.479				
Direct bilirubin (DBIL)	< 2.75	1(Ref.)							
	≥2.75	0.379	0.684	0.293	1.595				
Cholesterol (CHOL)	< 3.80	1(Ref.)							
	≥3.80	0.458	1.332	0.625	2.840				
Triglyceride (TG)	< 1.16	1(Ref.)							
	≥1.16	0.203	0.664	0.354	1.247				
Total protein (TP)	< 73.0	1(Ref.)							
	≥73.0	0.488	0.734	0.306	1.760				
Albumin (ALB)	< 44.1	1(Ref.)							
	≥44.1	0.111	0.442	0.162	1.207				
Globulin (G)	< 29.0	1(Ref.)							
	≥29.0	0.146	2.094	0.774	5.667				
Albumin/Globulin (A/G)	< 1.55	1(Ref.)							
	≥1.55	0.052	2.671	0.992	7.190				
Prealbumin (PAB)	< 27.0	1(Ref.)							
	≥27.0	0.364	1.412	0.670	2.977				
Carbohydrate antigen 125 (CA125)	< 10.57	1(Ref.)							
	≥10.57	0.461	1.326	0.626	2.811				
Carbohydrate antigen 153 (CA153)	< 13.01	1(Ref.)							
	≥13.01	0.311	1.423	0.719	2.819				
Carcinoembryonic antigen (CEA)	< 1.95	1(Ref.)							
	≥1.95	0.583	1.112	0.762	1.623				
D-Dimer (DD)	< 0.21	1(Ref.)							
	≥0.21	0.715	0.886	0.464	1.693				
Fibrinogen (FIB)	< 2.75	1(Ref.)							
	≥2.75	0.461	0.784	0.410	1.498				
White blood cell	< 5.45	1(Ref.)							
	≥5.45	0.376	1.187	0.812	1.733				
Neutrophils	< 3.23	1(Ref.)							
	≥3.23	0.062	1.437	0.981	2.103				
Lymphocyte	< 1.70	1(Ref.)							
	≥1.70	0.812	1.097	0.511	2.357				
Monocyte	< 0.35	1(Ref.)							
	≥0.35	0.356	1.361	0.707	2.622				
Platelet	< 233	1(Ref.)							
	≥233	0.137	0.607	0.314	1.173				
Type of surgery	Mastectomy	1(Ref.)							
	Breast-conserving surgery	0.894	1.106	0.252	4.843				
Pathological tumor size	≤2 cm	1(Ref.)							
	> 2 and ≤5 cm	0.230	0.490	0.153	1.571				
	> 5 cm	0.721	0.727	0.127	4.177				
Histologic grade	I	1(Ref.)							
	II	0.236	2.184	0.599	7.959				
	III	0.287	2.124	0.531	8.501				
Pathological T stage	T1 stage	1(Ref.)							

(*continued on next page*)

Table 3 (*continued*)

Characteristics	Group	Univariate		95%CI		Multivariate		95%CI	
		P	HR	Low	High	P	HR	Low	High
	T2 stage	0.122	3.012	0.744	12.197				
	T3 stage	0.431	2.158	0.318	14.662				
	T4 stage	0.370	2.202	0.392	12.380				
Pathological N stage	N0 stage	1(Ref.)							
	N1 stage	0.460	1.515	0.503	4.560				
	N2 stage	0.121	8.408	0.570	123.912				
	N3 stage	0.018	32.925	1.825	594.084				
Pathological TNM stage	I	1(Ref.)							
	II	0.195	6.986	0.369	132.221				
	III	0.225	4.340	0.406	46.437				
Total lymph nodes (TLN)	< 19	1(Ref.)							
	≥19	0.148	1.508	0.864	2.629				
Positive lymph nodes (PLN)	< 5	1(Ref.)							
	≥5	0.070	3.077	0.913	10.365				
Molecular subtype	Luminal A	1(Ref.)							
	Luminal B HER2+	0.007	0.017	0.001	0.325				
	Luminal B HER2-	0.617	1.454	0.336	6.296				
	HER2 enriched	0.001	0.006	0.000	0.119				
	Triple negative	0.411	0.427	0.056	3.255				
ER	Negative	1(Ref.)							
	Positive	0.368	0.636	0.237	1.704				
PR	Negative	1(Ref.)							
	Positive	0.139	2.091	0.788	5.548				
HER2	Negative	1(Ref.)							
	Positive	0.079	1.431	0.959	2.135				
Ki67	Negative	1(Ref.)							
	Positive	0.171	1.792	0.777	4.131				
AR	Negative	1(Ref.)							
	Positive	0.292	3.635	0.329	40.135				
CK5/6	Negative	1(Ref.)							
	Positive	0.340	1.676	0.580	4.846				
E-cad	Negative	1(Ref.)							
	Positive	0.245	1.705	0.694	4.191				
EGFR	Negative	1(Ref.)							
	Positive	0.604	0.690	0.170	2.807				
P53	Negative	1(Ref.)							
	Positive	0.757	1.117	0.555	2.246				
TOP2A	Negative	1(Ref.)				1(Ref.)			
	Positive	0.027	3.293	1.146	9.460	0.000	3.380	1.937	5.901
Lymph vessel invasion	Negative	1(Ref.)							
	Positive	0.092	1.738	0.913	3.308				
Neural invasion	Negative	1(Ref.)							
	Positive	0.455	1.299	0.654	2.581				
Postoperative chemotherapy	No	1(Ref.)							
	Yes	0.071	2.466	0.925	6.568				
Postoperative radiotherapy	No	1(Ref.)							
	Yes	0.103	0.495	0.213	1.153				
Postoperative endocrine therapy	No	1(Ref.)							
	Yes	0.193	1.928	0.717	5.187				
Postoperative targeted therapy	No	1(Ref.)							
	Yes	0.509	1.341	0.561	3.209				

Abbreviation: BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, Human Epidermal Growth Factor Receptor 2; AR, androgen receptor; CK5/6, Cytokeratin 5/6; E-cad, E-cadherin; EGFR, Epidermal Growth Factor Receptor; TOP2A, topoisomerase 2A.

was 0.693 (95%CI, 0.617–0.778), 10-year survival rate was 0.484 (95%CI, 0.395–0.593), 15-year survival rate was 0.234 (95%CI, 0.138–0.395) in low ALBI score group; and 1-year survival rate was 0.980 (95%CI, 0.941–1.000), 3-year survival rate was 0.790 (95% CI, 0.682–0.915), 5-year survival rate was 0.425 (95%CI, 0.301–0.599), 10-year survival rate was 0.103 (95%CI, 0.034–0.317) in high ALBI score group.

4.2. Establishment and validation of nomogram

Nomograms were considered a simple tool for providing personalized risk assessment for every enrolled patient. According to the potential prognostic factors discriminated in the multivariate analysis, we established two nomograms to individually predict different survival time of breast cancer patients with liver metastasis after surgery (Fig. 2A and B). The C-index for nomogram-based model by DFS was 0.611 (95%CI, 0.552–0.670) (Fig. S1A). And the C-index for nomogram-based model by OS was 0.721 (95%CI, 0.670–0.772)

Table 4
Univariate and multivariate survival analysis of overall survival in breast cancer patients with liver metastasis after surgery.

Characteristics	Group	Univariate		95%CI		Multivariate		95%CI	
		P	HR	Low	High	P	HR	Low	High
ALBI	Low	1(Ref.)				1(Ref.)			
	High	0.027	2.644	1.116	6.266	0.000	3.015	1.950	4.662
Age	< 49	1(Ref.)				1(Ref.)			
	≥49	0.006	2.934	1.361	6.326	0.378	1.212	0.790	1.859
Marital status	Married	1(Ref.)							
	Unmarried	0.946	1.097	0.077	15.713				
BMI	< 23.51	1(Ref.)							
	≥23.51	0.286	1.415	0.748	2.678				
Family history	No	1(Ref.)							
	Yes	0.589	0.840	0.445	1.583				
Menarche age	< 14	1(Ref.)				1(Ref.)			
	≥14	0.035	2.216	1.055	4.651	0.002	2.116	1.324	3.382
Menopause	No	1(Ref.)							
	Yes	0.102	0.453	0.175	1.172				
Alanine aminotransferase (ALT)	< 17	1(Ref.)							
	≥17	0.666	0.840	0.381	1.851				
Aspartate aminotransferase (AST)	< 20	1(Ref.)							
	≥20	0.959	0.979	0.436	2.198				
Lactic dehydrogenase (LDH)	< 166	1(Ref.)				1(Ref.)			
	≥166	0.029	2.209	1.086	4.493	0.005	1.851	1.203	2.847
γ-glutamyl transpeptidase (γ-GT)	< 17	1(Ref.)							
	≥17	0.505	1.253	0.646	2.430				
Direct bilirubin (DBIL)	< 2.75	1(Ref.)							
	≥2.75	0.475	0.761	0.359	1.612				
Cholesterol (CHOL)	< 3.80	1(Ref.)							
	≥3.80	0.377	1.420	0.652	3.093				
Triglyceride (TG)	< 1.16	1(Ref.)							
	≥1.16	0.162	0.650	0.355	1.190				
Total protein (TP)	< 73.0	1(Ref.)							
	≥73.0	0.869	0.929	0.389	2.220				
Albumin (ALB)	< 44.1	1(Ref.)							
	≥44.1	0.139	0.502	0.201	1.250				
Globulin(G)	< 29.0	1(Ref.)							
	≥29.0	0.629	0.809	0.342	1.913				
Albumin/Globulin (A/G)	< 1.55	1(Ref.)							
	≥1.55	0.491	1.349	0.576	3.158				
Prealbumin (PAB)	< 27.0	1(Ref.)							
	≥27.0	0.622	1.193	0.591	2.408				
Carbohydrate antigen 125 (CA125)	< 10.57	1(Ref.)							
	≥10.57	0.616	0.833	0.408	1.701				
Carbohydrate antigen 153 (CA153)	< 13.01	1(Ref.)							
	≥13.01	0.531	1.233	0.640	2.373				
Carcinoembryonic antigen (CEA)	< 1.95	1(Ref.)							
	≥1.95	0.369	0.741	0.386	1.424				
D-Dimer (DD)	< 0.21	1(Ref.)							
	≥0.21	0.544	0.815	0.422	1.577				
Fibrinogen (FIB)	< 2.75	1(Ref.)							
	≥2.75	0.298	0.723	0.392	1.333				
White blood cell	< 5.45	1(Ref.)							
	≥5.45	0.119	1.356	0.925	1.989				
Neutrophils	< 3.23	1(Ref.)				1(Ref.)			
	≥3.23	0.030	1.527	1.042	2.237	0.722	1.082	0.702	1.667
Lymphocyte	< 1.70	1(Ref.)				1(Ref.)			
	≥1.70	0.007	1.700	1.155	2.501	0.485	1.164	0.761	1.780
Monocyte	< 0.35	1(Ref.)				1(Ref.)			
	≥0.35	0.019	1.583	1.077	2.326	0.015	1.670	1.105	2.524
Platelet	< 233	1(Ref.)							
	≥233	0.556	0.822	0.428	1.578				
Type of surgery	Mastectomy	1(Ref.)							
	Breast-conserving surgery	0.997	0.997	0.210	4.727				
Pathological tumor size	≤2 cm	1(Ref.)							
	> 2 and ≤5 cm	0.248	0.510	0.163	1.599				
	> 5 cm	0.856	1.172	0.212	6.473				
Histologic grade	I	1(Ref.)							
	II	0.209	2.291	0.628	8.359				
	III	0.613	1.441	0.350	5.935				
Pathological T stage	T1 stage	1(Ref.)							

(*continued on next page*)

Table 4 (*continued*)

Characteristics	Group	Univariate		95%CI		Multivariate		95%CI	
		P	HR	Low	High	P	HR	Low	High
	T2 stage	0.275	2.135	0.547	8.322				
	T3 stage	0.559	1.842	0.238	14.261				
	T4 stage	0.013	8.755	1.587	48.307				
Pathological N stage	N0 stage	1(Ref.)							
	N1 stage	0.228	1.969	0.655	5.920				
	N2 stage	0.136	7.056	0.542	91.903				
	N3 stage	0.025	25.620	1.513	433.911				
Pathological TNM stage	I	1(Ref.)							
	II	0.102	9.057	0.648	126.674				
	III	0.110	5.844	0.669	51.054				
Total lymph nodes (TLN)	< 19	1(Ref.)							
	≥19	0.433	0.859	0.588	1.255				
Positive lymph nodes (PLN)	< 5	1(Ref.)							
	≥5	0.335	1.834	0.534	6.295				
Molecular subtype	Luminal A	1(Ref.)							
	Luminal B HER2+	0.241	0.190	0.012	3.059				
	Luminal B HER2-	0.592	1.505	0.338	6.701				
	HER2 enriched	0.125	0.090	0.004	1.947				
	Triple negative	0.968	1.042	0.146	7.406				
ER	Negative	1(Ref.)				1(Ref.)			
	Positive	0.002	10.058	2.271	44.549	0.001	3.272	1.649	6.494
PR	Negative	1(Ref.)							
	Positive	0.216	1.898	0.688	5.239				
HER2	Negative	1(Ref.)							
	Positive	0.209	5.440	0.388	76.259				
Ki67	Negative	1(Ref.)							
	Positive	0.849	1.083	0.475	2.469				
AR	Negative	1(Ref.)							
	Positive	0.936	0.902	0.073	11.119				
CK5/6	Negative	1(Ref.)							
	Positive	0.491	1.461	0.498	4.287				
E-cad	Negative	1(Ref.)							
	Positive	0.284	1.616	0.672	3.886				
EGFR	Negative	1(Ref.)							
	Positive	0.601	0.671	0.151	2.988				
P53	Negative	1(Ref.)							
	Positive	0.069	1.952	0.948	4.018				
TOP2A	Negative	1(Ref.)				1(Ref.)			
	Positive	0.046	3.021	1.021	8.934	0.002	2.443	1.393	4.282
Lymph vessel invasion	Negative	1(Ref.)							
	Positive	0.318	1.385	0.731	2.626				
Neural invasion	Negative	1(Ref.)							
	Positive	0.052	3.208	0.990	10.398				
Postoperative chemotherapy	No	1(Ref.)							
	Yes	0.741	0.923	0.572	1.487				
Postoperative radiotherapy	No	1(Ref.)							
	Yes	0.060	0.463	0.207	1.032				
Postoperative endocrine therapy	No	1(Ref.)							
	Yes	0.784	1.146	0.431	3.049				
Postoperative targeted therapy	No	1(Ref.)							
	Yes	0.826	0.912	0.401	2.073				

Abbreviation: BMI, body mass index; ER, estrogen receptor; PR, progesterone receptor; HER2, Human Epidermal Growth Factor Receptor 2; AR, androgen receptor; CK5/6, Cytokeratin 5/6; E-cad, E-cadherin; EGFR, Epidermal Growth Factor Receptor; TOP2A, topoisomerase 2A.

(Fig. S1B). Moreover, the calibration curves of DFS at 1-year, 3-year, and 5-year after surgery performed that the best consistency between the actual and predicted observations (Fig. 3A–C). And the calibration curves of OS at 1-year, 3-year, 5-year, and 10-year after surgery indicated that the best agreement between the actual and predicted observations (Fig. 3D–G). In addition, the decision curve analysis of DFS at 3-year after surgery demonstrated that the constructed nomograms had better predictive value than ALBI score (Fig. 4A–D). And the decision curve analysis of OS at 3-year, 5-year, and 10-year after surgery demonstrated that the established nomograms had better predictive value than ALBI score (Fig. 4E–H). Furthermore, time-dependent receiver operating characteristic (TDROC) analysis performed that the plots of area under the receiver operating characteristic curves (AUROCs) for ALBI score in breast cancer patients with liver metastasis after surgery for survival time from 1 year to 15 years after the start of follow-up. TDROC analysis indicated that the AUROCs at 1-year, 3-year, 5-year, and 10-year of DFS after surgery of follow-up were 0.573, 0.539, 0.574, 0.561 for the ALBI score; and 1-year, 3-year, 5-year, 10-year, and 15-year of OS after surgery of follow-up were 0.614, 0.535, 0613, 0.658, 0.644 for the ALBI score. The ALBI score indicated that the AUROCs for survival time had the highest value at 5-year point (95%CI: 49.17%–

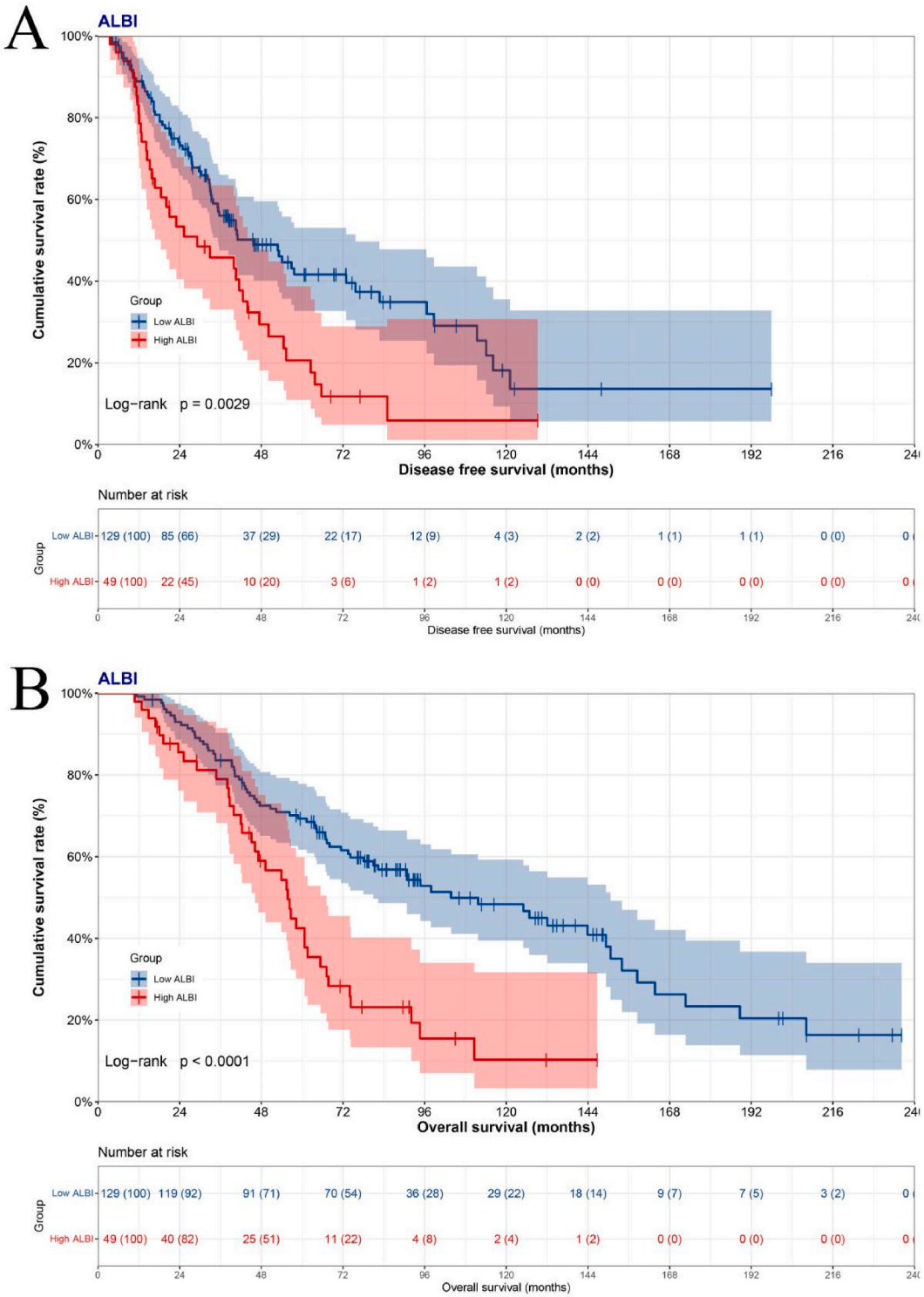

Fig. 1. Kaplan-Meier survival plots comparing disease free survival (DFS) and overall survival (OS) in breast cancer patients with liver metastasis after surgery (A for DFS, B for OS).

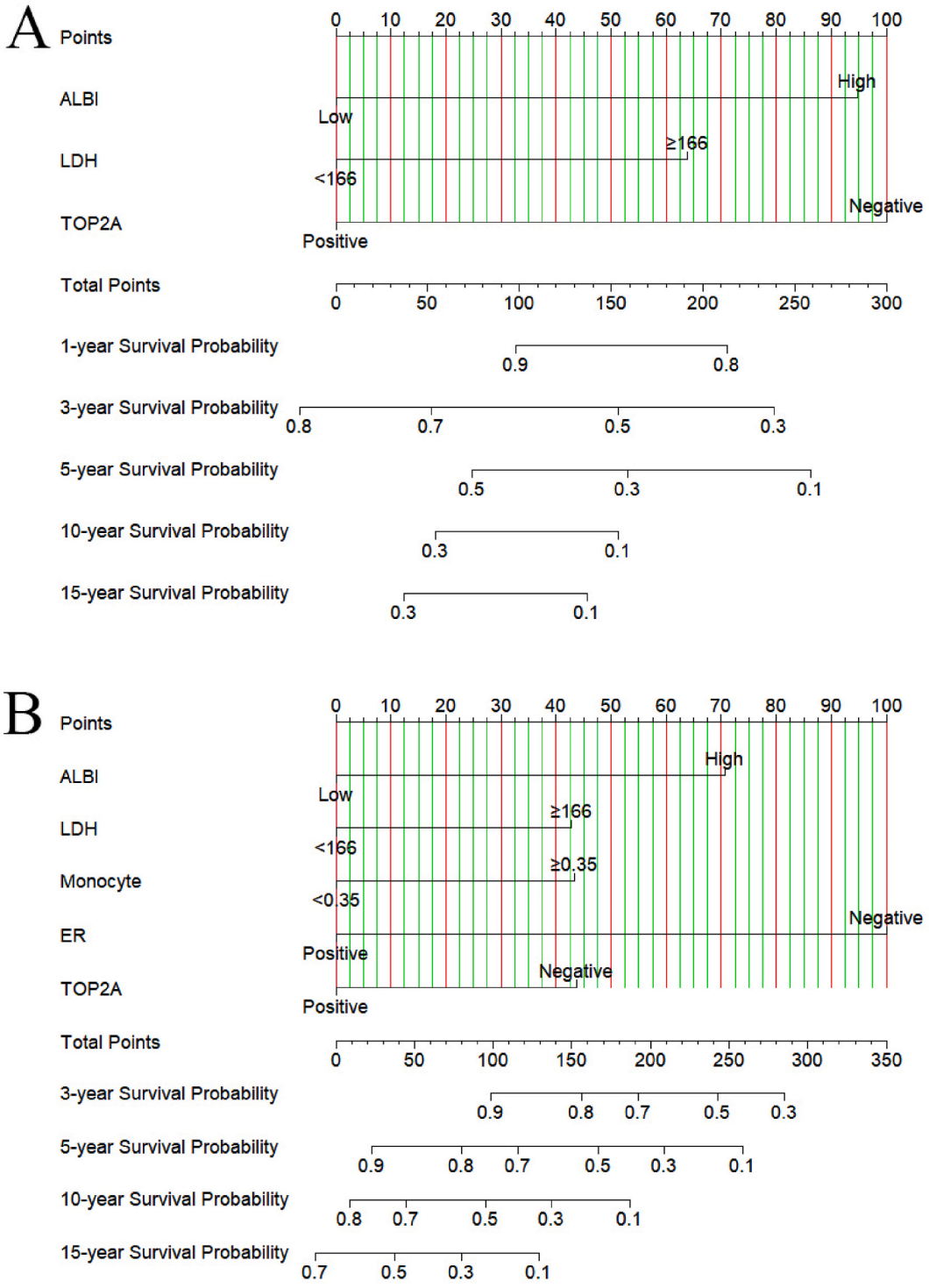

Fig. 2. The established of ALBI-based nomograms in breast cancer patients with liver metastasis after surgery (A, nomogram of disease free survival; B, nomogram of overall survival).

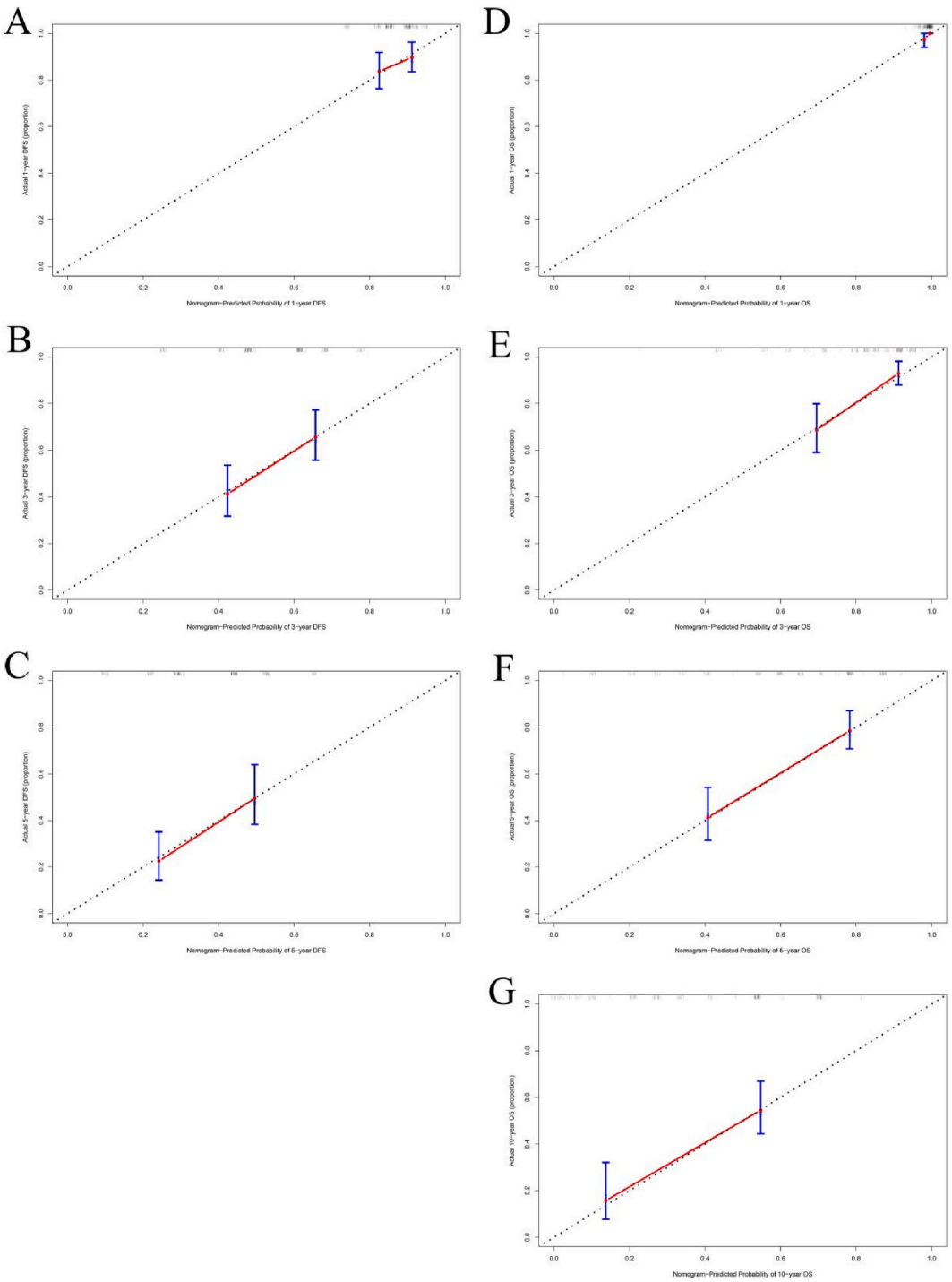

Fig. 3. The calibration curves for ALBI-nomogram model in predicting different survival time. A) 1-year DFS, B) 3-year DFS, C) 5-year DFS, D) 1-year OS, E) 3-year OS, F) 5-year OS, G) 10-year OS.

65.67 %) for DFS (Fig. 5A and B), and at 10-year point (95%CI, 59.20%–72.38 %) for OS (Fig. 5C and D).

4.3. Subgroup analyses to evaluate the effects of the ALBI score on survival

Then, we conducted subgroup analyses to evaluate the impacts of ALBI score on survival according to the menopause. Kaplan-Meier curves revealed that the ALBI score was associated with DFS (Log rank: $p = 0.031$) and OS (Log rank: $p = 0.00024$) in menopause status

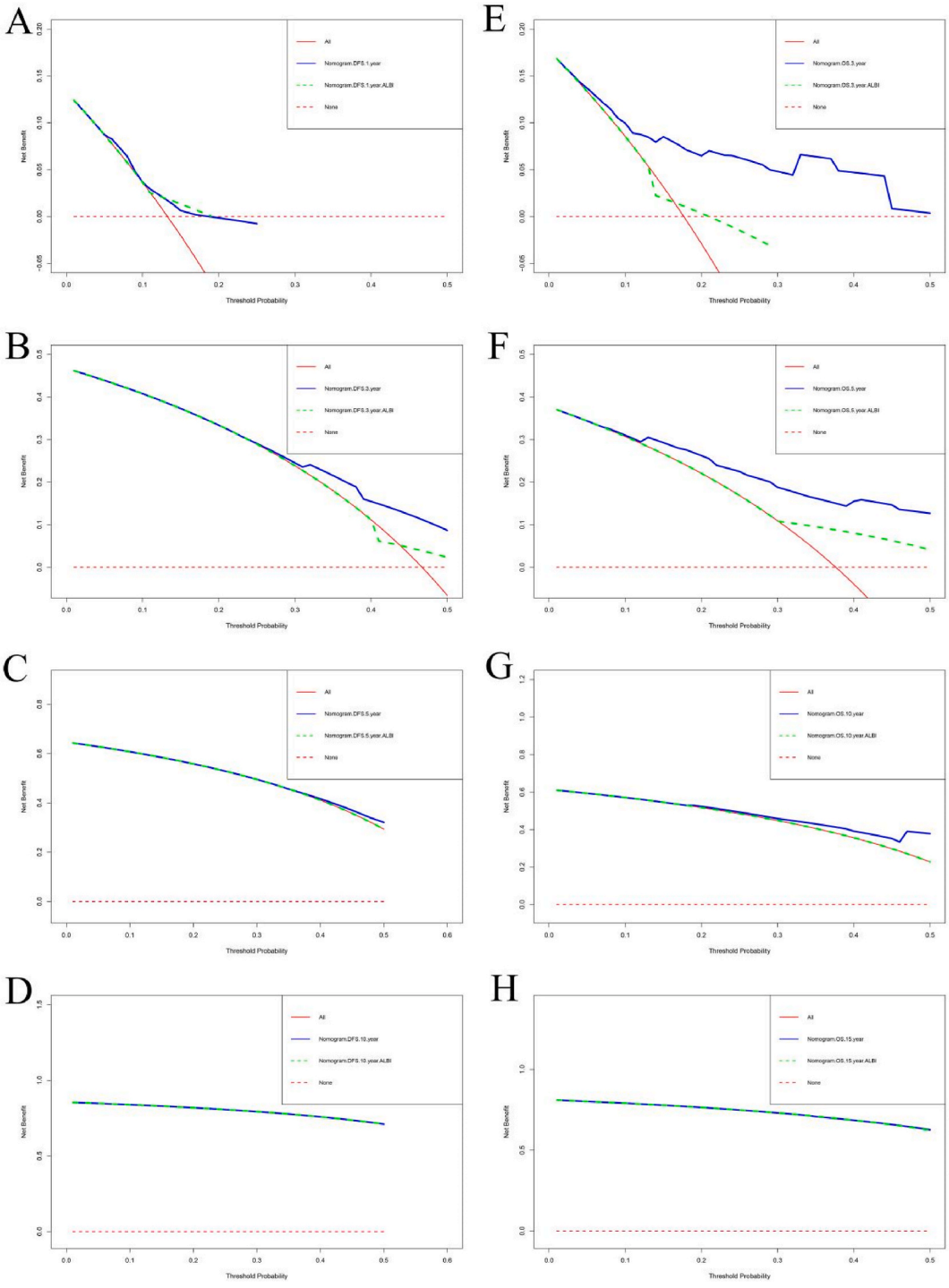

Fig. 4. The decision curve analysis for the ALBI-nomogram and ALBI score model in evaluating the benefits for different survival time. A) 1-year DFS, B) 3-year DFS, C) 5-year DFS, D) 10-year DFS, E) 3-year OS, F) 5-year OS, G) 10-year OS, H) 15-year OS.

(Figs. S2A–B). The postmenopausal patients with breast cancer with high ALBI score had poor prognosis and survival time. Moreover, we also analyzed the effects of ALBI grade on survival according to the histological grade. Kaplan-Meier curves shown that the ALBI score was significantly associated with DFS (Log rank: $p = 0.0033$) and OS (Log rank: $p = 0.00072$) in different histological grade (Figs. S3A–B). The higher histological grade breast cancer patients with high ALBI score had worse prognosis and shorter survival time. In addition, we also compared the impacts of ALBI score on survival by molecular subtype. Kaplan-Meier curves indicated that the ALBI

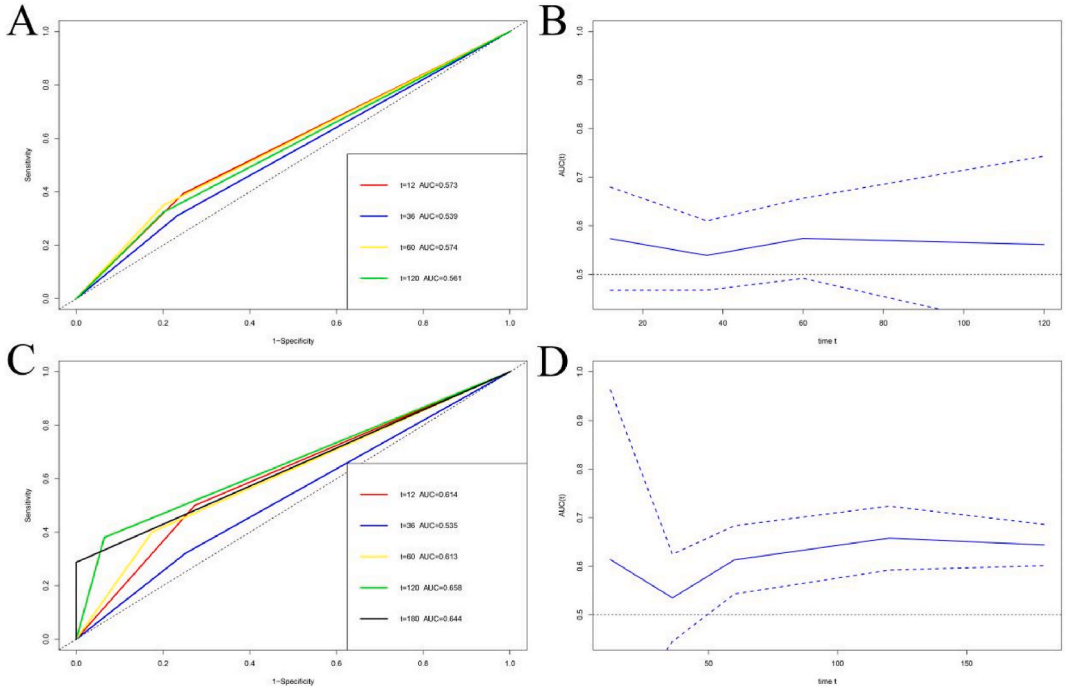

Fig. 5. Time-dependent receiver operating characteristic (TDROC) analyzed the plots of area under the receiver operating characteristic curves (AUROCs) for ALBI score in breast cancer patients with liver metastasis after surgery of followup. A) Time-dependent AUROCs for DFS, B) 95%CI changes of AUROCs for DFS, C) Time-dependent AUROCs for OS, D) 95%CI changes of AUROCs for OS.

score was dramatically associated with DFS (Log rank: $p = 0.00052$) and OS (Log rank: $p < 0.0001$) in molecular subtype of breast cancer (Figs. S4A–B).

5. Discussion

Breast cancer primarily metastasizes to bone, lung, liver and brain by way of circulation; wherein, the liver is the third most usual distant metastasis site of breast cancer [17]. It is worth noting that the incidence of liver metastasis is second only to lung and bone metastasis in an autopsy study, and liver metastasis accounts for 20 %–35 % of the deaths of metastatic breast cancer patients [18]. In addition, liver metastasis can lead to treatment resistance and higher mortality rates. The breast cancer patients with liver metastasis have poor prognosis and short median survival time [19]. Studies have proved that the median survival time of these patients without any therapy was about 4–8 months compared to 13–31 months after systemic therapy [20–22]. At present, it is hard to accurately predict the occurrence of liver metastasis from breast cancer. Although several prognostic scores had been reported to be related to prognosis in breast cancer patients, it was still unclear whether these markers reflect prognosis in both the short-term and long-term [23,24].

Johnson and his colleagues inaugurated the ALBI grade to estimate liver function [7]. After being proven to have prognostic benefits for liver cancer patients in 2015, there is increasing interest in the prognostic role of ALBI grade [7,25,26]. The ALBI is composed of albumin and bilirubin, and is measured by routine blood test. Albumin is synthesized in the liver and the decline in its level indicates malnutrition and liver synthesis dysfunction [27]. Additionally, an increase in serum bilirubin concentration usually determines varying degrees of liver dysfunction [28]. Hiraoka A and his colleagues designed a multicenter study including 6649 liver cancer patients treated from 2000 to 2017 and found that ALBI grade had prognostic predictive value and stratification ability [29]. Of late, in a single-center study by Koh HH and his colleagues analyzing 1015 patients with colorectal cancer, the ALBI grade was a significant prognostic factor, and the combination of ALBI and myosteatosis shown additional value in judging the survival rate of CRC patients [30]. Moreover, Takada K and his colleagues had analyzed 452 patients with advanced or recurrent NSCLC who received anti-PD-1 therapy and found that the ALBI grade was an independent prognostic factor for progression-free survival and overall survival [11].

In the current study, we reported that the ALBI score was a potential predictor of DFS and OS in breast cancer patients with liver metastasis after surgery. The median DFS and OS in low ALBI score group were longer than in high ALBI score group. A pooled analysis of two randomized trials indicated that higher ALBI grade was related to worse PFS and OS among patients with colorectal liver metastases treated with first-line systemic therapy [31]. Another study pointed out that a higher pretreatment ALBI grade was associated with worse PFS and OS in pancreatic cancer patients with liver metastasis treated with chemotherapy in the first-line setting, and it could help the treatment outcomes [32]. Our findings were consistent with previous reports, and our study also

explored the clinical impact of ALBI grade in breast cancer patients with liver metastasis after surgery.

In the current queue, the ALBI score was significantly associated with menopause, histologic grade, positive lymph nodes, molecular subtype, albumin, cholesterol, and total protein (Tables 1 and 2), suggesting that the ALBI score was related to a bias from these clinical factors. With regards to menopause, the post-menopausal estrone activates EMT genes to stimulate breast cancer metastasis [33]. In this study, the results also indicated that the postmenopausal patients with high ALBI score had worse prognosis and shorter survival time. A previous study noted that the histological grade was positively associated with the proliferation and metastasis ability of tumor cells, and the higher the histological grade of breast cancer, the higher the risk of metastasis [34]. The results in our study also indicated that ALBI score was significantly related to histological grade of breast cancer, and the higher the histological grade of breast cancer with high ALBI score had poor prognosis and survival by Kaplan-Meier curves. Another study suggested that the probability of liver metastasis in HER2 positive subtype and triple negative subtype were significantly higher than that in HR+/HER2 subtypes [35]. Our present results also proved that triple-negative subtype and HER2 enriched subtype patients with high ALBI group had shorter survival time, in accordance with this published study. In addition, the albumin, cholesterol and total protein often used to assess liver function and nutritional status [36,37]. The patients with low albumin or high cholesterol level usually had poor prognosis, consistent with previously published researches [38,39].

We established effective ALBI-based nomograms for individualized assessment of breast cancer patients with liver metastasis after surgery. These nomograms had distinctive characteristics that integrate ALBI, LDH, monocyte, ER, and TOP2A. The results of calibration curves and decision curve analysis shown that ALBI-based nomograms were repeatedly and reliably predict the prognosis of breast cancer patients with liver metastasis after surgery, and these models might assist in individualized risk stratification and the development of individualized follow-up and treatment strategies. ROC analysis is typically used to appraise the discriminant power of continuous variables on binary disease outcomes. Nevertheless, it is hard to contrast the prognosis determined applying ordinary ROC analysis because outcomes are time dependent [40]. The time-dependent ROC curves have been innovated for evaluating the predictive power of diagnostic markers for time dependent disease outcomes. In this study, the prognosis of breast cancer patients with liver metastasis after surgery was also performed by the time-dependent ROC analysis. The results indicated that the AUROCs for survival time by ALBI score had the highest value at 5-year point for DFS and at 10-year point for OS.

It is worth noting that this research also has several limitations. First, this was a single-center retrospective study, the number of patients was relatively small, which may have some selection bias. Secondly, these established nomograms were using retrospective data, thus prospective cohort studies should be performed for further validation. Finally, the ALBI score's suitability to predict the prognosis of breast cancer patients with liver metastasis after surgery who receive other therapy needs further study.

6. Conclusion

In summary, tumor metastasis after radical surgery for breast cancer is a critical and natural complication. Our study indicates that the ALBI score has high prognostic ability for DFS and OS in breast cancer with liver metastasis after surgery. Our findings suggest that the advantage of ALBI score is that objectivity, easy to implement, without invasive procedures. We also construct nomograms, which is a energetic tool to predict subsequent liver metastasis in breast cancer patients after surgery. These models will help us in discriminating patients at high risks of liver metastasis, thereupon then we can design relevant trials for these patients. However, larger studies are needed to determine whether our results can be applied to other subgroups of breast patients.

Funding

This research was supported by grants from the National Nature Science Foundation of China (No.82173328), Hubei Province Postdoctoral Innovation Research Post Fund Project (No.0106540096), Open Fund for the Key Laboratory of Organ Transplantation of Ministry of Education and National Health Commission (No.2021QYKF03), Tongji Hospital Cultivation Project (No.2022B03), Chen Xiao-ping Foundation for the Development of Science and Technology of Hubei province, Youth Science Special Fund (No. CXPJJH123001-2308).

This retrospective single center study was conducted in accordance with the amended Declaration of Helsinki, and was approved by the ethics committee of Cancer Hospital Chinese Academy of Medical Sciences (Approved no.82173328).

Informed consent statement

The enrolled patients provided written informed consent for using their data in this retrospective study.

Data availability statement

The material supporting the conclusion of this article has been included within the article.

CRediT authorship contribution statement

Li Chen: Writing – review & editing, Writing – original draft, Resources, Funding acquisition, Formal analysis. **Chunlei Tan:** Writing – review & editing, Investigation, Data curation. **Qingwen Li:** Writing – review & editing, Data curation. **Zhibo Ma:** Data curation. **Meng Wu:** Investigation. **Xiaosheng Tan:** Supervision, Methodology. **Tiangen Wu:** Formal analysis. **Jinwen Liu:**

Conceptualization. **Jing Wang:** Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

No.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e21772.

References

[1] R.L. Siegel, K.D. Miller, N.S. Wagle, A. Jemal, Cancer statistics, 2023, CA Cancer J Clin 73 (1) (2023) 17–48, https://doi.org/10.3322/caac.21763.
[2] N.F. Pondé, D. Zardavas, M. Piccart, Progress in adjuvant systemic therapy for breast cancer, Nat. Rev. Clin. Oncol. 16 (1) (2019) 27–44, https://doi.org/10.1038/s41571-018-0089-9.
[3] V. Padmanaban, I. Krol, Y. Suhail, B.M. Szczerba, N. Aceto, J.S. Bader, A.J. Ewald, E-cadherin is required for metastasis in multiple models of breast cancer, Nature 573 (7774) (2019) 439–444, https://doi.org/10.1038/s41586-019-1526-3.
[4] Z. Abduyev, K. Altundag, CA-125 might be good predictive tumor biomarker for earlier detection of serosal metastases including the ovarian metastasis in high-risk invasive lobular breast cancer, J BUON 24 (4) (2019) 1735.
[5] J. Zhang, Q. Wei, D. Dong, L. Ren, The role of TPS, CA125, CA15-3 and CEA in prediction of distant metastasis of breast cancer, Clin. Chim. Acta 523 (2021) 19–25, https://doi.org/10.1016/j.cca.2021.08.027.
[6] L. Jia, G. Li, N. Ma, A. Zhang, Y. Zhou, L. Ren, D. Dong, Soluble POSTN is a novel biomarker complementing CA153 and CEA for breast cancer diagnosis and metastasis prediction, BMC Cancer 22 (1) (2022) 760, https://doi.org/10.1186/s12885-022-09864-y.
[7] P.J. Johnson, S. Berhane, C. Kagebayashi, S. Satomura, M. Teng, H.L. Reeves, J. O'Beirne, R. Fox, A. Skowronska, D. Palmer, et al., Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach-the ALBI grade, J. Clin. Oncol. 33 (6) (2015) 550–558, https://doi.org/10.1200/JCO.2014.57.9151.
[8] A. Hiraoka, T. Kumada, K. Michitaka, M. Kudo, Newly proposed ALBI grade and ALBI-T score as tools for assessment of hepatic function and prognosis in hepatocellular carcinoma patients, Liver Cancer 8 (5) (2019) 312–325, https://doi.org/10.1159/000494844.
[9] A.W.H. Chan, J. Zhong, S. Berhane, H. Toyoda, A. Cucchetti, K. Shi, T. Tada, C.C.N. Chong, B.D. Xiang, L.Q. Li, et al., Development of pre and post-operative models to predict early recurrence of hepatocellular carcinoma after surgical resection, J. Hepatol. 69 (6) (2018) 1284–1293, https://doi.org/10.1016/j.jhep.2018.08.027.
[10] R.K. Kelley, R. Miksad, I. Cicin, Y. Chen, H.J. Klümpen, S. Kim, Z.Z. Lin, J. Youkstetter, S. Hazra, S. Sen, et al., Efficacy and safety of cabozantinib for patients with advanced hepatocellular carcinoma based on albumin-bilirubin grade, Br. J. Cancer 126 (4) (2022) 569–575, https://doi.org/10.1038/s41416-021-01532-5.
[11] K. Takada, S. Takamori, M. Shimokawa, G. Toyokawa, S. Shimamatsu, F. Hirai, T. Tagawa, T. Okamoto, M. Hamatake, Y. Tsuchiya-Kawano, et al., Assessment of the albumin-bilirubin grade as a prognostic factor in patients with non-small-cell lung cancer receiving anti-PD-1-based therapy, ESMO Open 7 (1) (2022), 100348, https://doi.org/10.1016/j.esmoop.2021.100348.
[12] T. Imamura, Y. Okamura, T. Sugiura, T. Ito, Y. Yamamoto, R. Ashida, K. Ohgi, S. Otsuka, K. Uesaka, Clinical significance of preoperative albumin-bilirubin grade in pancreatic cancer, Ann. Surg Oncol. 28 (11) (2021) 6223–6235, https://doi.org/10.1245/s10434-021-09593-9.
[13] S. Kaneko, M. Kurosaki, K. Tsuchiya, Y. Yasui, K. Inada, S. Kirino, K. Yamashita, L. Osawa, Y. Hayakawa, S. Sekiguchi, et al., Prognosis of intrahepatic cholangiocarcinoma stratified by albumin-bilirubin grade, Hepatol. Res. 51 (8) (2021) 902–908, https://doi.org/10.1111/hepr.13673.
[14] C. Zhu, X. Wang, S. Chen, X. Yang, J. Sun, B. Pan, W. Zhang, X. Chen, Y. Huang, Efficacy of the preoperative albumin-bilirubin grade for predicting survival and outcomes of postoperative chemotherapy for advanced gastric cancer, Cancer Manag. Res. 12 (2020) 11921–11932, https://doi.org/10.2147/CMAR.S279782.
[15] D. Kim, J.H. Lee, E.S. Cho, S.J. Shin, H.S. Lee, H.H. Koh, K.Y. Lee, J. Kang, Clinical significance of combining preoperative and postoperative albumin-bilirubin score in colorectal cancer, Cancer Res Treat (2023), https://doi.org/10.4143/crt.2022.1444, 10.4143/crt.2022.1444.
[16] Q. Zuo, N.H. Park, J.K. Lee, Z. Madak Erdogan, Liver metastatic breast cancer: epidemiology, dietary interventions, and related metabolism, Nutrients 14 (12) (2022) 2376, https://doi.org/10.3390/nu14122376.
[17] A. Yang, W. Xiao, S. Zheng, Y. Kong, Y. Zou, M. Li, F. Ye, X. Xie, Predictive nomogram of subsequent liver metastasis after mastectomy or breast-conserving surgery in patients with nonmetastatic breast cancer, Cancer Control 28 (2021), 1073274821997418, https://doi.org/10.1177/1073274821997418.
[18] M.C. Cummings, P.T. Simpson, L.E. Reid, J. Jayanthan, J. Skerman, S. Song, A.E. McCart Reed, J.R. Kutasovic, A.L. Morey, L. Marquart, et al., Metastatic progression of breast cancer: insights from 50 years of autopsies, J. Pathol. 232 (1) (2014) 23–31, https://doi.org/10.1002/path.4288.
[19] N.S. Rashid, J.M. Grible, C.V. Clevenger, J.C. Harrell, Breast cancer liver metastasis: current and future treatment approaches, Clin. Exp. Metastasis 38 (3) (2021) 263–277, https://doi.org/10.1007/s10585-021-10080-4.
[20] A. Ruiz, R. van Hillegersberg, S. Siesling, C. Castro-Benitez, M. Sebagh, D.A. Wicherts, K.M. de Ligt, L. Goense, S. Giacchetti, D. Castaing, et al., Surgical resection versus systemic therapy for breast cancer liver metastases: results of a European case matched comparison, Eur. J. Cancer 95 (2018) 1–10, https://doi.org/10.1016/j.ejca.2018.02.024.
[21] E. Sadot, S.Y. Lee, C.T. Sofocleous, S.B. Solomon, M. Gönen, T.P. Kingham, P.J. Allen, R.P. DeMatteo, W.R. Jarnagin, C.A. Hudis, et al., Hepatic resection or ablation for isolated breast cancer liver metastasis: a case-control study with comparison to medically treated patients, Ann. Surg. 264 (1) (2016) 147–154, https://doi.org/10.1097/SLA.0000000000001371.
[22] V. Lucidi, A. Bohlok, G. Liberale, M. Bez, D. Germanova, F. Bouazza, P. Demetter, D. Larsimont, P. Aftimos, N.R. Smoll, et al., Extended time interval between diagnosis and surgery does not improve the outcome in patients operated for resection or ablation of breast cancer liver metastases, Eur. J. Surg. Oncol. 46 (2) (2020) 229–234, https://doi.org/10.1016/j.ejso.2019.10.016.
[23] J. Wang, Y. Li, W. Fu, Y. Zhang, J. Jiang, Y. Zhang, X. Qi, Prognostic nomogram based on immune scores for breast cancer patients, Cancer Med. 8 (11) (2019) 5214–5222, https://doi.org/10.1002/cam4.2428.
[24] L. Li, Z.P. Liu, Detecting prognostic biomarkers of breast cancer by regularized Cox proportional hazards models, J. Transl. Med. 19 (1) (2021) 14, https://doi.org/10.1186/s12967-021-03180-y.

[25] D.J. Pinato, R. Sharma, E. Allara, C. Yen, T. Arizumi, K. Kubota, D. Bettinger, J.W. Jang, C. Smirne, Y.W. Kim, et al., The ALBI grade provides objective hepatic reserve estimation across each BCLC stage of hepatocellular carcinoma, J. Hepatol. 66 (2) (2017) 338–346, https://doi.org/10.1016/j.jhep.2016.09.008.
[26] A.W.H. Chan, H.H.W. Leung, C.C.N. Chong, S.L. Chan, Validating the ALBI grade: its current and future use in HCC prognostication, J. Hepatol. 66 (3) (2017) 661–663, https://doi.org/10.1016/j.jhep.2016.10.037.
[27] F. Chicco, S. Magrì, A. Cingolani, D. Paduano, M. Pesenti, F. Zara, F. Tumbarello, E. Urru, A. Melis, L. Casula, M.C. Fantini, P. Usai, Multidimensional impact of mediterranean diet on IBD patients, Inflamm. Bowel Dis. 27 (1) (2021) 1–9, https://doi.org/10.1093/ibd/izaa097.
[28] D.J. Pinato, R. Sharma, C. Citti, H. Platt, M. Ventura-Cots, E. Allara, T.Y. Chen, A. Dalla Pria, M. Jain, B. Mínguez, et al., The albumin-bilirubin grade uncovers the prognostic relationship between hepatic reserve and immune dysfunction in HIV-associated hepatocellular carcinoma, Aliment. Pharmacol. Ther. 47 (1) (2018) 95–103, https://doi.org/10.1111/apt.14356.
[29] A. Hiraoka, T. Kumada, K. Tsuji, K. Takaguchi, E. Itobayashi, K. Kariyama, H. Ochi, K. Tajiri, M. Hirooka, N. Shimada, et al., Validation of modified ALBI grade for more detailed assessment of hepatic function in hepatocellular carcinoma patients: a multicenter analysis, Liver Cancer 8 (2) (2019) 121–129, https://doi.org/10.1159/000488778.
[30] H.H. Koh, E.S. Cho, J.H. Lee, S.J. Shin, H.S. Lee, E.J. Park, S.H. Baik, K.Y. Lee, J. Kang, Association of albumin-bilirubin grade and myosteatosis with its prognostic significance for patients with colorectal cancer, Ann. Surg Oncol. 29 (6) (2022) 3868–3876, https://doi.org/10.1245/s10434-022-11445-z.
[31] O. Abdel-Rahman, Prognostic value of baseline ALBI score among patients with colorectal liver metastases: a pooled analysis of two randomized trials, Clin. Colorectal Cancer 18 (1) (2019) e61–e68, https://doi.org/10.1016/j.clcc.2018.09.008.
[32] A. Sakin, S. Sahin, A. Sakin, M.M. Atci, N. Yasar, S. Arici, C. Geredeli, F. Karatas, S. Cihan, Assessment of pretreatment albumin-bilirubin grade in pancreatic cancer patients with liver metastasis, J BUON 25 (4) (2020) 1941–1946.
[33] R. Qureshi, M. Picon-Ruiz, M. Sho, D. Van Booven, V. Nunes de Paiva, A.B. Diaz-Ruano, T.A. Ince, J. Slingerland, Estrone, the major postmenopausal estrogen, binds ERa to induce SNAI2, epithelial-to-mesenchymal transition, and ER+ breast cancer metastasis, Cell Rep. 41 (7) (2022), 111672, https://doi.org/10.1016/j.celrep.2022.111672.
[34] A. Purushotham, E. Shamil, M. Cariati, O. Agbaje, A. Muhidin, C. Gillett, A. Mera, K. Sivanadiyan, M. Harries, R. Sullivan, et al., Age at diagnosis and distant metastasis in breast cancer–a surprising inverse relationship, Eur. J. Cancer 50 (10) (2014) 1697–1705, https://doi.org/10.1016/j.ejca.2014.04.002.
[35] L. Ji, L. Cheng, X. Zhu, Y. Gao, L. Fan, Z. Wang, Risk and prognostic factors of breast cancer with liver metastases, BMC Cancer 21 (1) (2021) 238, https://doi.org/10.1186/s12885-021-07968-5.
[36] P.M. Ridker, D.L. Bhatt, A.D. Pradhan, R.J. Glynn, J.G. MacFadyen, S.E. Nissen, PROMINENT, REDUCE-IT, and STRENGTH Investigators. Inflammation and cholesterol as predictors of cardiovascular events among patients receiving statin therapy: a collaborative analysis of three randomised trials, Lancet 401 (10384) (2023) 1293–1301, https://doi.org/10.1016/S0140-6736(23)00215-5.
[37] D. Sousa-Catita, C. Ferreira-Santos, P. Mascarenhas, C. Oliveira, R. Madeira, C.A. Santos, C. André, C. Godinho, L. Antunes, J. Malnutrition Fonseca, Cancer stage and gastrostomy timing as markers of poor outcomes in gastrostomy-fed head and neck cancer patients, Nutrients 15 (3) (2023) 662, https://doi.org/10.3390/nu15030662.
[38] Y. Yoshino, A. Taguchi, T. Shimizuguchi, Y. Nakajima, M. Takao, T. Kashiyama, A. Furusawa, N. Kino, T. Yasugi, A low albumin to globulin ratio with a high serum globulin level is a prognostic marker for poor survival in cervical cancer patients treated with radiation based therapy, Int. J. Gynecol. Cancer 29 (1) (2019) 17–22, https://doi.org/10.1136/ijgc-2018-000025.
[39] L. Chen, Y. Qi, X. Kong, Z. Su, Z. Wang, X. Wang, Y. Du, Y. Fang, X. Li, J. Wang, Nutritional risk index predicts survival in patients with breast cancer treated with neoadjuvant chemotherapy, Front. Nutr. 8 (2022), 786742, https://doi.org/10.3389/fnut.2021.786742.
[40] A.N. Kamarudin, T. Cox, R. Kolamunnage-Dona, Time-dependent ROC curve analysis in medical research: current methods and applications, BMC Med. Res. Methodol. 17 (1) (2017) 53, https://doi.org/10.1186/s12874-017-0332-6.