BMC Gastroenterology

RESEARCH

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Comprehensive analysis of risk factors and nomogram development for predicting hepatic metastasis following radical resection of adenocarcinoma of the esophagogastric junction

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Abstract

Background Adenocarcinoma of the esophagogastric junction (AEG) often presents with subtle early symptoms and delayed diagnosis, frequently resulting in liver metastasis and a poor prognosis. This study aimed to investigate the primary risk factors influencing postoperative liver metastasis in AEG and to develop a simple predictive model to facilitate clinical risk stratification and individualized follow-up strategies.

Methods This retrospective study analyzed data from 524 patients with AEG who underwent radical resection, with patients randomly divided into a training group (368 cases) and a validation group (156 cases). Clinical and pathological information was collected, and independent factors significantly associated with postoperative liver metastasis were identified using univariate and multivariate Cox regression analyses. Based on these findings, a nomogram model was constructed to predict the 1-year and 3-year liver metastasis-free survival rates, and the model's predictive performance and clinical utility were evaluated using the C-index, ROC curves, and calibration curves.

Results Multivariate analysis revealed that thoracoabdominal surgery, higher N stage (N1 and N2/N3), moderate-to-poor differentiation, the presence of vascular tumor thrombus, intestinal type according to Lauren classification, and P53 status were independent risk factors for postoperative liver metastasis. The nomogram model based on these six indicators demonstrated high predictive accuracy in both the training group (C-index = 0.966) and the validation group (C-index = 0.976), with ROC AUCs for both the 1-year and 3-year predictions exceeding 0.96 and favorable calibration curves, confirming the model's strong predictive efficacy.

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Conclusions The predictive model developed in this study can effectively assess the risk of postoperative liver metastasis in patients with AEG, thereby providing a scientific basis for postoperative monitoring and individualized treatment, with the potential to improve patient outcomes in clinical practice.

Introduction

Adenocarcinoma of the esophagogastric junction (AEG) is a malignancy at the esophagus - stomach junction [1–3]. Over the past half-century, the incidence and mortality of gastric cancer outside the esophagogastric junction have declined, while those of AEG have risen [4]. The prognosis for AEG is generally worse than for gastric cancer outside the esophagogastric junction [5]. Distinct from lower esophageal and other gastric cancers, it mainly affects elderly males and is predominantly of the intestinal type according to Lauren classification. Often diagnosed at an advanced stage, it has a low five-year survival rate [6]. AEG's risk factors include obesity, gastroesophageal reflux disease, and smoking [7]. In contrast, gastric cancer outside the esophagogastric junction is linked to Helicobacter pylori infection and high - salt diets [8]. AEG shows no or negative correlation with H. pylori [4]. Symptoms like dysphagia, retrosternal pain, weight loss, and fatigue typically appear late due to the cancer's asymptomatic early stage, facilitated by the strong peristaltic and extensibility of the lower esophagus [8].

AEG metastasizes mainly via lymphatic, implantation, direct invasion, and hematogenous routes [9]. Its location allows metastasis to thoracic or abdominal lymph nodes, with high lymphatic spread. Implantation involves cancer cells settling in the rectum, bladder, and ovaries. Direct invasion affects nearby organs like the esophagus, liver, and omentum. Hematogenous spread, common to distant organs such as the liver, lungs, bones, and brain, with the liver being the most frequent site, is significant [10]. Liver metastasis in gastric cancer occurs in 5–14% of cases [11], more so in cardia than non-cardia cancer [12]. It's the top cause of death in advanced stages, with a median survival of 9 months (95%*CI*: 6.5–9.5 months) [10]. Postoperative liver metastasis often shortens survival, highlighting the need for identifying independent prognostic factors for metastasis-free survival.

Current research on AEG prognosis usually focuses on recurrence and metastasis, and the influencing factors are mostly related to the lymph node stage and its impact on postoperative recurrence and metastasis [13, 14]. However, in clinical practice, postoperative recurrence and metastasis result from the combined effect of multiple factors. The TNM staging system is a commonly used clinical tool for predicting patient prognosis [15–17], but it has limitations. The prognosis of cancer patients is often also related to factors such as age, degree of differentiation, and surgical approach. Therefore, a more comprehensive and intuitive tool is needed to assess the prognosis of cancer patients.

Thus, this study aims to construct a nomogram model for predicting liver metastasis after surgery for AEG, providing clinicians with a powerful visual tool and tumor markers to enhance the accuracy of predicting postoperative liver metastasis. This, in turn, can facilitate the development of personalized treatment strategies for patients, thereby improving survival rates and prognosis.

Methods

Study subjects

This study included 524 patients with AEG who underwent radical surgical resection at the Fourth Affiliated Hospital of Henan University of Science and Technology (Anyang Tumor Hospital, Anyang, Henan, China) between January 2017 and September 2020. They were divided into two groups based on the presence of liver metastasis after surgery: the liver metastasis group (58 cases) and the non-liver metastasis group (466 cases).

This study was approved by the hospital's medical ethics committee (2024–069). It followed the principles of the declaration of Helsinki. Written informed consent was obtained from all participants or their guardians

Inclusion Criteria.

1. Age > 18 years, both sexes;
2. Definitive diagnosis of AEG based on gastroscopy, upper gastrointestinal imaging, surgical records, and postoperative pathology.

Exclusion Criteria.

1. Patients with other primary malignant tumors besides AEG;
2. Patients with missing critical information, such as clinical data;
3. Patients who already had liver metastasis at the time of radical surgery for AEG;
4. Patients who died from non-tumor-related causes.

The process of data collection and exclusion is detailed in Fig. 1.

Data collection

General clinical data were collected for the included patients, including age, sex, surgical approach, surgical method, T stage, N stage, tumor length, degree of

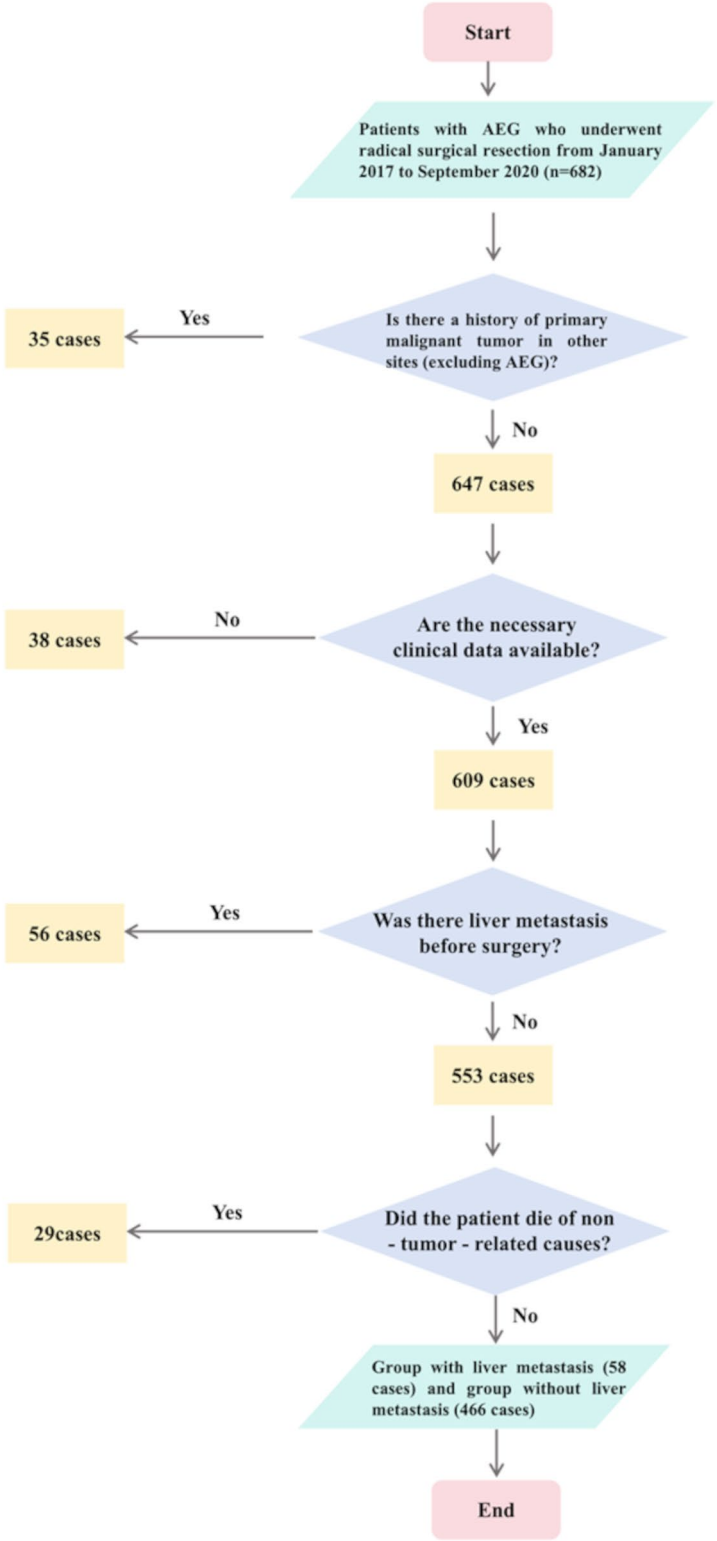

Fig. 1 Flowchart for data collection and data exclusion

differentiation, Lauren classification, P53, Her2, Ki-67, presence of vascular tumor thrombus, and presence of neural invasion, totaling 14 indicators, as well as imaging and pathological examination results. In this study, the cutoff value for Ki-67 was set at 25%.

Surgical approaches

1. Transabdominal Approach: Entering through the abdomen, suitable for tumors on the gastric side or below the gastroesophageal junction. It is less invasive and easier to perform, facilitating tumor resection and lymph node dissection.
2. Transthoracic Approach: Entering through the chest, ideal for high-position esophageal tumors. It provides better exposure of the esophagus and surrounding tissues but is more invasive with a longer recovery time.
3. Combined Approach: Using both transabdominal and transthoracic paths, applied for complex or extensive tumors. However, it is more complex and demands higher physical condition from the patient.

Surgical Methods.

1. Proximal Gastrectomy: Removing the upper part of the stomach while preserving part of the gastric body and antrum. It is used for localized tumors, requiring esophagogastrostomy post-surgery.
2. Total Gastrectomy: Removing the entire stomach and replacing its function with the jejunum. It is suitable for large tumors or those with extensive adhesion to surrounding tissues, necessitating gastrointestinal reconstruction post-surgery.

Follow-Up Methods.

1. Follow-up methods in this study included: outpatient follow-up, telephone follow-up, and inpatient re-evaluation when necessary. Follow-up content included medical history collection, physical examination, laboratory tests, and imaging studies, with a focus on assessing postoperative recovery, signs of recurrence or metastasis, and the occurrence of complications.
2. Follow-up intervals after discharge: Patients were followed up every 3 months for the first 2 years after surgery, every 6 months between 2 and 5 years post-surgery, and annually after 5 years. Additional follow-up and further testing were promptly arranged if patients exhibited symptoms related to recurrence or metastasis, such as upper abdominal pain, weight loss, or jaundice.
3. Imaging and laboratory tests performed during follow-up:

Abdominal CT or MRI: Used to evaluate the presence of metastatic lesions in the liver and other abdominal organs. Enhanced CT or MRI (e.g., with liver-specific contrast agents) was recommended to improve detection of small lesions.

Serum tumor marker tests: Including carcinoembryonic antigen (CEA) and carbohydrate antigen 19 – 9 (CA19-9), with dynamic monitoring of trends to assist in early detection of recurrence or metastasis.

Esophagogastroduodenoscopy (EGD): Performed annually to examine the anastomosis and residual gastric mucosa, and to rule out local recurrence or complications such as anastomotic ulcers.

Chest CT: Conducted every 6 to 12 months to assess for pulmonary or mediastinal lymph node metastasis.

PET-CT or bone scan when indicated: Performed if there was suspicion of systemic metastasis or bone involvement.

Statistical analysis

SPSS 25.0 and R 4.3.0 software were employed for the statistical analysis of the data in this study. The 524 patients with AEG were randomly divided into a training group (368 cases) and a validation group (156 cases) at a ratio of 7:3. Continuous data that followed a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and inter-group comparisons were conducted using independent samples t-test. Continuous data that did not conform to a normal distribution were represented by the median (first quartile, third quartile) [*M* (*Q1*, *Q3*)], and inter-group comparisons were performed using rank-sum test. Categorical data were presented as frequencies and percentages, and inter-group comparisons were carried out using the chi-square test or Fisher's exact test. Univariate and multivariate Cox regression analyses were used to identify independent influencing factors. Variables with $P<0.25$ in the univariate analysis were included in the multivariate analysis, and a nomogram prediction model for the risk of postoperative liver metastasis in patients with AEG was constructed based on factors with $P<0.05$. The validation group was used for internal validation of the model, and the consistency and accuracy of the nomogram were evaluated using calibration curves and the area under the receiver operating characteristic (ROC) curve (AUC). Decision curve analysis (DCA) was utilized to assess the clinical practicality and effectiveness of the nomogram model.

Results

General clinical and pathological characteristics of patients with AEG

This study enrolled a total of 524 patients with AEG, comprising 418 males and 106 females, with a male-to-female ratio of 3.9:1. The age range was from 35 to 88 years, with a median age (*M*) of 65.0 years (*Q1*, *Q3*: 61.0, 70.0 years). Among these patients, 58 (11.1%) developed liver metastasis after radical surgery, while 466 (88.9%) did not. Metastasis to the left lobe of the liver was observed in 8 cases (13.8%), to the right lobe in 9 cases (15.5%), and to both lobes in 41 cases (70.7%). The liver metastases were present as a single nodule in 19 cases (32.8%) and as multiple nodules in 39 cases (67.2%). The incidence of liver metastasis was 7.4% at 1 year after surgery and 11.1% at 3 years after surgery. The median follow-up time for all patients was 46.6 months (95%*CI*: 45.2–48.0 months), and the median liver metastasis-free survival was not reached.

Using R 4.3.0 software, 368 patients (70%) were randomly selected from the 524 patients who underwent radical surgery for AEG to form the training group, which included 291 males and 77 females with a median age (*M*) of 65 years (*Q1*, *Q3*: 61.0, 70.0 years). The remaining 156 patients (30%) constituted the validation group, comprising 127 males and 29 females with a median age (*M*) of 65 years (*Q1*, *Q3*: 60.0, 71.0 years). In this study, a comparison of the baseline characteristics between the training and validation groups revealed no statistically significant differences in any of the baseline parameters ($P > 0.05$). See Table 1 for details.

Analysis of risk factors for hepatic metastasis after surgery for AEG

Univariate Cox analysis

Univariate analysis revealed significant differences between the liver metastasis and non-metastasis groups in T stage, N stage, tumor length, differentiation, vascular tumor thrombus, and nerve invasion (all $P < 0.05$). However, no statistically significant differences were observed between the two groups in terms of gender, age, surgical approach, surgical method, Lauren classification, P53, Her2, and Ki-67 status (all $P > 0.05$). See Table 2 for details.

Multivariate Cox analysis

Given that the differences in results from the univariate analysis may not fully reflect the true effect of each factor on the outcome, and that the true effects could be underestimated or obscured, the criteria for inclusion in the multivariate Cox regression analysis were relaxed to $P < 0.25$ to effectively prevent the omission of important variables [18]. The results revealed that surgical approach (transabdominal: *HR* = 0.871, 95%*CI*: 0.346 ~ 2.192; thoracoabdominal: *HR* = 9.472, 95%*CI*: 1.769 ~ 50.723), N stage (N1: *HR* = 5.376, 95%*CI*: 0.628 ~ 45.993; N2, N3: *HR* = 10.633, 95%*CI*: 1.188 ~ 95.197), degree of differentiation (moderately differentiated: *HR* = 65.340, 95%*CI*: 5.124 ~ 833.225; poorly differentiated: *HR* = 4278.607, 95%*CI*: 241.069 ~ 75938.601), presence of vascular tumor thrombus (*HR* = 4.933, 95%*CI*: 1.887 ~ 12.892), Lauren classification (mixed type: *HR* = 0.592, 95%*CI*: 0.235 ~ 1.491; intestinal type: *HR* = 9.607, 95%*CI*: 3.480 ~ 26.524), and P53 status (*HR* = 0.240, 95%*CI*: 0.103 ~ 0.558) were predictive factors for the risk of hepatic metastasis after radical surgery for AEG (Table 3).

Development of a predictive model

Based on the six key predictive factors identified through Cox regression analysis, this study constructed a nomogram model to predict the 1-year and 3-year survival rates without hepatic metastasis (Fig. 2). The nomogram illustrates that the degree of differentiation has the greatest impact on the prognosis of survival without hepatic metastasis after surgery for AEG, followed by Lauren classification, surgical approach, N stage, presence of vascular tumor thrombus, and P53 status. Each indicator is assigned a corresponding risk score, and by calculating the total risk score, the respective 1-year and 3-year survival rates without hepatic metastasis can be determined.

The concordance index (C-index) is a metric in survival analysis that measures the consistency between the predicted results of a Cox model and the actual outcomes, commonly used to assess the predictive accuracy of prognostic models for cancer patients [19, 20]. The C-index ranges from 0.5 to 1.0, where 0.5 indicates random prediction with no predictive value, and 1.0 signifies perfect agreement between predictions and actual outcomes. A model with a C-index of 0.50–0.70 is considered to have low accuracy; a C-index of 0.71–0.90 indicates moderate accuracy; and a C-index above 0.90 denotes a high-accuracy model. The C-index for the training group of this predictive model was 0.966 (95%*CI*: 0.957–0.975), and for the validation group, it was 0.976 (95%*CI*: 0.969–0.983), both being above 0.9.

The Receiver Operating Characteristic (ROC) curve is a statistical tool commonly used in medical diagnostics and evaluation of test accuracy to measure the strength of a model's generalization capability. The Area Under the Curve (AUC) values for the 1-year prediction in the training group were 0.972 (95%*CI*: 0.952–0.992), and for the 3-year prediction, 0.991 (95%*CI*: 0.982–1.001). For the validation group, the 1-year AUC value was 0.960 (95%*CI*: 0.919–1.002), and the 3-year AUC value was 0.976 (95%*CI*: 0.948–1.005). The ROC curves for both the training and validation groups were close to the top left corner with AUCs greater than 0.9. See Fig. 3A and B.

Table 1 Comparison of clinicopathological characteristics between the training and validation groups

Features	Training group($n=368$)	Validation group($n=156$)	*P*-value
Age[$M(Q_1,Q_3)$,years]	65.0(61.0, 70.0)	65.0(60.0, 71.0)	0.833
Gender[cases(%)]			0.625
Female	77(20.9)	29(18.6)	
Male	291(79.1)	127(81.4)	
Surgical approach[cases(%)]			0.625
Transabdominal	112(30.4)	41(26.3)	
Transthoracic	239(65.0)	108(69.2)	
Combined	17(4.6)	7(4.5)	
Surgical method[cases(%)]			0.361
Proximal Gastrectomy	342(92.9)	149(95.5)	
Total Gastrectomy	26(7.1)	7(4.5)	
T staging [cases(%)]			1
T1、T2	81(22.0)	35(22.4)	
T3、T4	287(78.0)	121(77.6)	
N staging [cases (%)]			0.503
N0	140(38.0)	63(40.4)	
N1	101(27.4)	35(22.4)	
N2、N3	127(34.5)	58(37.2)	
Tumor length [cases (%)]			0.823
< 5 cm	202(54.9)	88(56.4)	
≥ 5 cm	166(45.1)	68(43.6)	
Differentiation degree [cases (%)]			0.899
Well-differentiated	148(40.2)	61(39.1)	
Moderately differentiated	191(51.9)	81(51.9)	
Poorly differentiated	29(7.9)	14(9.0)	
Vascular tumor thrombus [cases (%)]			0.958
None	262(71.2)	110(70.5)	
Present	106(28.8)	46(29.5)	
Neural invasion [cases (%)]			0.275
None	186(50.5)	70(44.9)	
Present	182(49.5)	86(55.1)	
Lauren classification [cases (%)]			0.881
Diffuse type	57(15.5)	26(16.7)	
Intestinal type	199(54.1)	81(51.9)	
Mixed type	112(30.4)	49(31.4)	
P53 [cases (%)]			0.406
Negative	72(19.6)	25(16.0)	
Positive	296(80.4)	131(84.0)	
Her2 [cases (%)]			0.119
Negative	315(85.6)	142(91.0)	
Positive	53(14.4)	14(9.0)	
Ki-67 [cases (%)]			0.402
Negative	28(7.6)	8(5.1)	
Positive	340(92.4)	148(94.9)	
Outcome [cases (%)]			1.000
No liver metastasis	327(88.9)	139(89.1)	
Liver metastasis	41(11.1)	17(10.9)	

The calibration curve is commonly used to assess the precision of a model in predicting individual clinical outcomes. The calibration curve derived from the model in this study closely approximates the ideal curve, indicating a high degree of calibration. See Fig. 3C.

DCA is a relatively new method for evaluating model clinical practicality, which plots a curve with different threshold probabilities on the horizontal axis and the corresponding net benefit on the vertical axis [21–23]. It can analyze aspects of clinical practicality that common

Table 2 Summary table of univariate Cox analysis results

Item	Regression Coefficient	HR Value	Standard Error	Wald	*P*-value	95%CI for HR	
						Lower Limit	Upper Limit
Age (years)	-0.008	0.992	0.020	-0.407	0.684	0.953	1.032
Gender							
Female		*Re*					
Male	-0.064	0.938	0.377	-0.170	0.865	0.448	1.965
Surgical approach							
Transabdominal		*Re*					
Transthoracic	0.780	2.181	0.419	1.864	0.062	0.96	4.954
Thoracoabdominal	1.168	3.214	0.690	1.691	0.091	0.831	12.433
Surgical Method							
Proximal Gastrectomy		*Re*					
Total Gastrectomy	0.405	1.499	0.527	0.768	0.442	0.534	4.207
T staging							
T1、T2		*Re*					
T3、T4	1.781	5.938	0.725	2.457	0.014	1.434	24.591
N staging							
N0		*Re*					
N1	2.466	11.777	1.061	2.325	0.020	1.473	94.167
N2、N3	3.716	41.097	1.016	3.659	0.000	5.614	300.839
Tumor Length							
< 5 cm		*Re*					
≥ 5 cm	0.716	2.045	0.320	2.235	0.025	1.092	3.831
Differentiation Degree							
Well-differentiated		*Re*					
Moderately-differentiated	2.241	9.401	1.041	2.153	0.031	1.222	72.313
Poorly-differentiated	6.137	462.618	1.037	5.918	0.000	60.616	3530.653
Vascular Tumor Thrombus							
None		*Re*					
Present	2.660	14.295	0.415	6.404	0.000	6.333	32.267
Neural Invasion							
None		*Re*					
Present	0.961	2.615	0.343	2.800	0.005	1.334	5.126
Lauren Classification							
Diffuse Type		*Re*					
Mixed Type	-0.450	0.637	0.441	-1.021	0.307	0.269	1.513
Intestinal Type	-0.494	0.610	0.401	-1.231	0.218	0.278	1.340
P53							
Negative		*Re*					
Positive	-0.579	0.560	0.343	-1.687	0.092	0.286	1.098
Her2							
Negative		*Re*					
Positive	0.196	1.216	0.415	0.472	0.637	0.539	2.744
Ki-67							
Negative		*Re*					
Positive	0.030	1.031	0.600	0.051	0.959	0.318	3.340

Note: *HR* stands for Hazard Ratio; *Re* stands for Reference Item

statistical metrics such as sensitivity, specificity, area under the ROC curve, and calibration cannot consider. The DCA results for 1-year and 3-year liver metastasis-free survival show that the net benefit is greater than 0 across the entire range of threshold probabilities. See Fig. 3D.

Discussion

This retrospective study analyzed data from 524 patients with AEG and identified key risk factors for postoperative hepatic metastasis. A nomogram model was developed to predict 1- and 3-year liver metastasis-free survival. The independent risk factors identified were

Table 3 Summary table of multivariate Cox analysis results

Influencing factors	Regression Coefficient	HR Value	Standard Error	Wald	*P*-value	95% CI for HR	
						Lower Limit	Upper Limit
Surgical approach							
Transabdominal		*Re*					
Transthoracic	-0.138	0.871	0.471	-0.293	0.770	0.346	2.192
Thoracoabdominal	2.248	9.472	0.856	2.626	0.009	1.769	50.723
T staging							
T1、T2		*Re*					
T3、T4	0.363	1.438	0.848	0.428	0.668	0.273	7.578
N staging							
N0		*Re*					
N1	1.682	5.376	1.095	1.536	0.125	0.628	45.993
N2、N3	2.364	10.633	1.118	2.114	0.035	1.188	95.197
Tumor Length							
< 5 cm		*Re*					
≥ 5 cm	0.427	1.533	0.366	1.168	0.243	0.749	3.138
Differentiation Degree							
Well-differentiated		*Re*					
Moderately-differentiated	4.180	65.340	1.299	3.218	0.001	5.124	833.225
Poorly-differentiated	8.361	4278.607	1.468	5.698	0.000	241.069	75938.601
Vascular Tumor Thrombus							
None		*Re*					
Present	1.596	4.933	0.490	3.256	0.001	1.887	12.892
Neural Invasion							
None		*Re*					
Present	-0.567	0.567	0.430	-1.318	0.187	0.244	1.318
Lauren Classification							
Diffuse Type		*Re*					
Mixed Type	-0.525	0.592	0.472	-1.113	0.266	0.235	1.491
Intestinal Type	2.263	9.607	0.518	4.367	0.000	3.480	26.524
P53							
Negative		*Re*					
Positive	-1.429	0.240	0.431	-3.314	0.001	0.103	0.558

Note: *HR* stands for Hazard Ratio; *Re* stands for Reference Item

thoracoabdominal surgery, higher N stage (N1 and N2/N3), moderate-to-poor differentiation, vascular tumor thrombus, intestinal type per Lauren classification, and positive P53 status. The nomogram demonstrated exceptional predictive accuracy in both training and validation groups, with C-indices of 0.966 and 0.976, respectively, and AUCs exceeding 0.96. Calibration curves were near-ideal, and DCA confirmed net clinical benefit across all probability thresholds. This model offers clinicians a reliable tool to identify high-risk patients, enabling personalized postoperative surveillance and treatment strategies, such as increased imaging frequency or adjuvant therapy for high-risk cases, to improve patient outcomes.

Currently, the vast majority of literature focuses on the recurrence risk and overall survival of gastric cancer, with very few studies addressing metastasis after surgery for AEG. This study indicates that postoperative liver metastasis of AEG is influenced by multiple prognostic factors. For example, the choice of surgical approach is very important. The "Chinese Expert Consensus on Surgical Treatment of Adenocarcinoma of the Esophagogastric Junction (2024)" recommends the transthoracic approach for Siewert type I, the transabdominal or retrosternal approach for Siewert type III, while the choice of surgical approach for Siewert type II remains controversial [24]. There is currently little literature discussing the impact of surgical approach on the risk of postoperative liver metastasis in AEG. In the multivariate COX analysis of this study (Table 3), there was a significant difference in the risk of postoperative liver metastasis between the thoracoabdominal combined approach and the other two surgical approaches, meaning the thoracoabdominal combined approach had a higher risk of postoperative liver metastasis, while there was no significant difference in the risk of postoperative liver metastasis between the transthoracic approach and the transabdominal approach. In addition, N staging reflects the status of lymph node metastasis; the higher

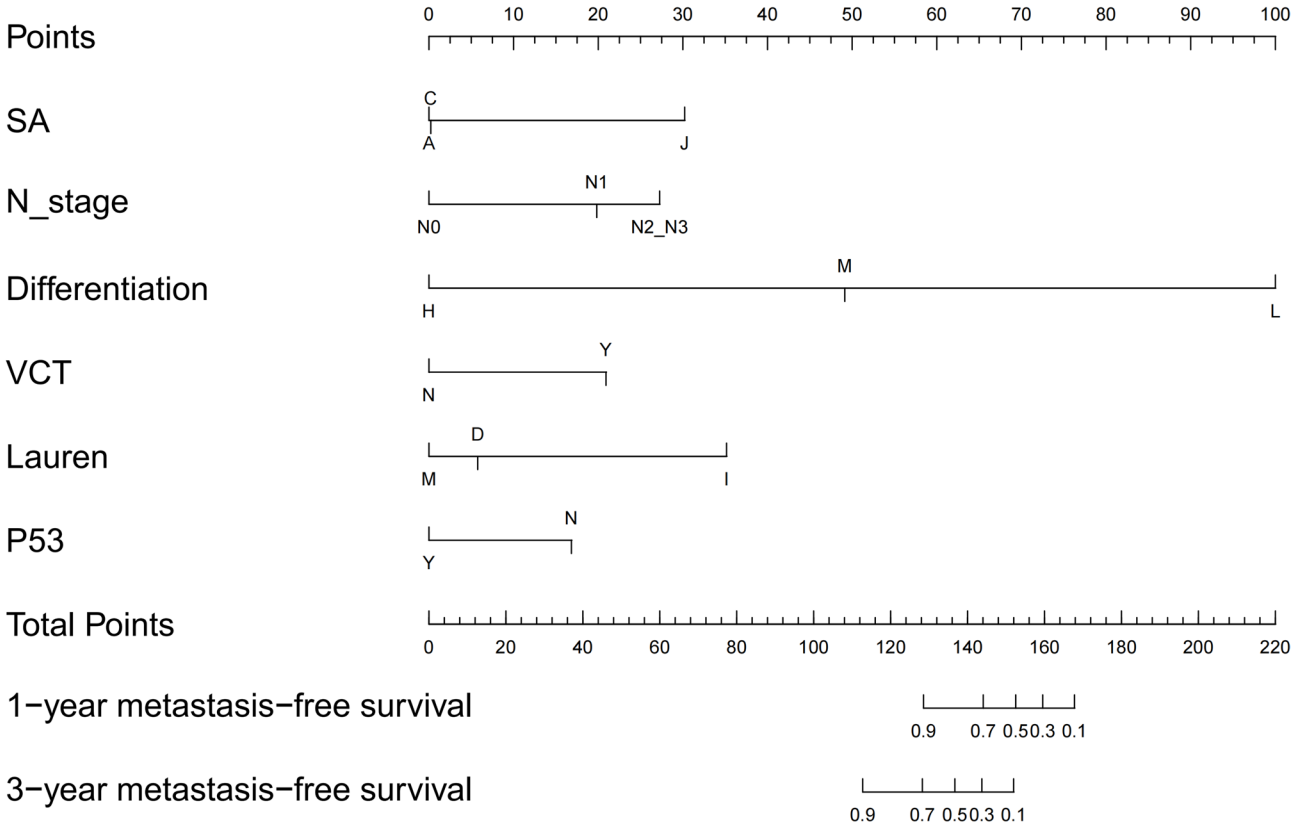

Fig. 2 Nomogram of predicting the liver-metastasis of AEG

the N stage, the more extensive the possible spread of the tumor through the lymphatic system, increasing the risk of liver metastasis and shortening the liver metastasis-free survival time. Although liver metastasis primarily occurs via hematogenous spread, lymphatic metastasis is also one of its pathways. Previous studies have confirmed that N staging is a risk factor for gastric cancer liver metastasis, and patients with high N staging are more likely to develop liver metastasis, thus close monitoring is crucial [25–27]. Poorer differentiation degree indicates more aggressive tumor biological behavior, higher metastatic potential, and worse prognosis, and is significantly associated with shorter liver metastasis-free survival time [28]. Intravascular tumor emboli are microscopic metastatic foci formed by cancer cells invading the vascular and lymphatic systems, and are an important indicator of tumor metastasis, predicting a high risk of tumor recurrence and progression, and are of significant importance for assessing metastasis risk and prognosis; this study found that patients with intravascular tumor emboli had an increased risk of postoperative liver metastasis and shortened liver metastasis-free survival time. Lauren classification (intestinal type, diffuse type, mixed type) can reflect the biological and pathological characteristics of gastric cancer and is widely used clinically; some studies have shown that the risk of liver metastasis is higher in intestinal type gastric cancer than in diffuse type [29–32], and the results of this study are similar, finding that the risk of liver metastasis in diffuse type AEG is lower than in mixed type. The P53 gene plays an important role in maintaining genomic stability, and mutations can lead to uncontrolled cell proliferation, tumor progression, and affect invasive and metastatic ability. Therefore, P53 gene abnormalities are often associated with shorter liver metastasis-free survival time. A study found that P53 expression level was significantly correlated with distant metastasis-free survival in prostate cancer [33], but this study found that patients with negative P53 expression had longer liver metastasis-free survival, and the exact correlation requires more evidence for confirmation. In summary, these prognostic factors collectively determine the patient's liver metastasis-free survival time by influencing tumor growth, invasion, and metastatic potential. In clinical practice, identifying and evaluating these factors is crucial for formulating personalized treatment strategies and improving patient prognosis.

Furthermore, as a visual predictive tool, the nomogram has been widely used in the field of oncology in recent years. However, up to now, there have been no reports of a nomogram model for predicting postoperative hepatic metastasis in AEG. The innovation of this study lies in the fact that it not only clarifies the independent

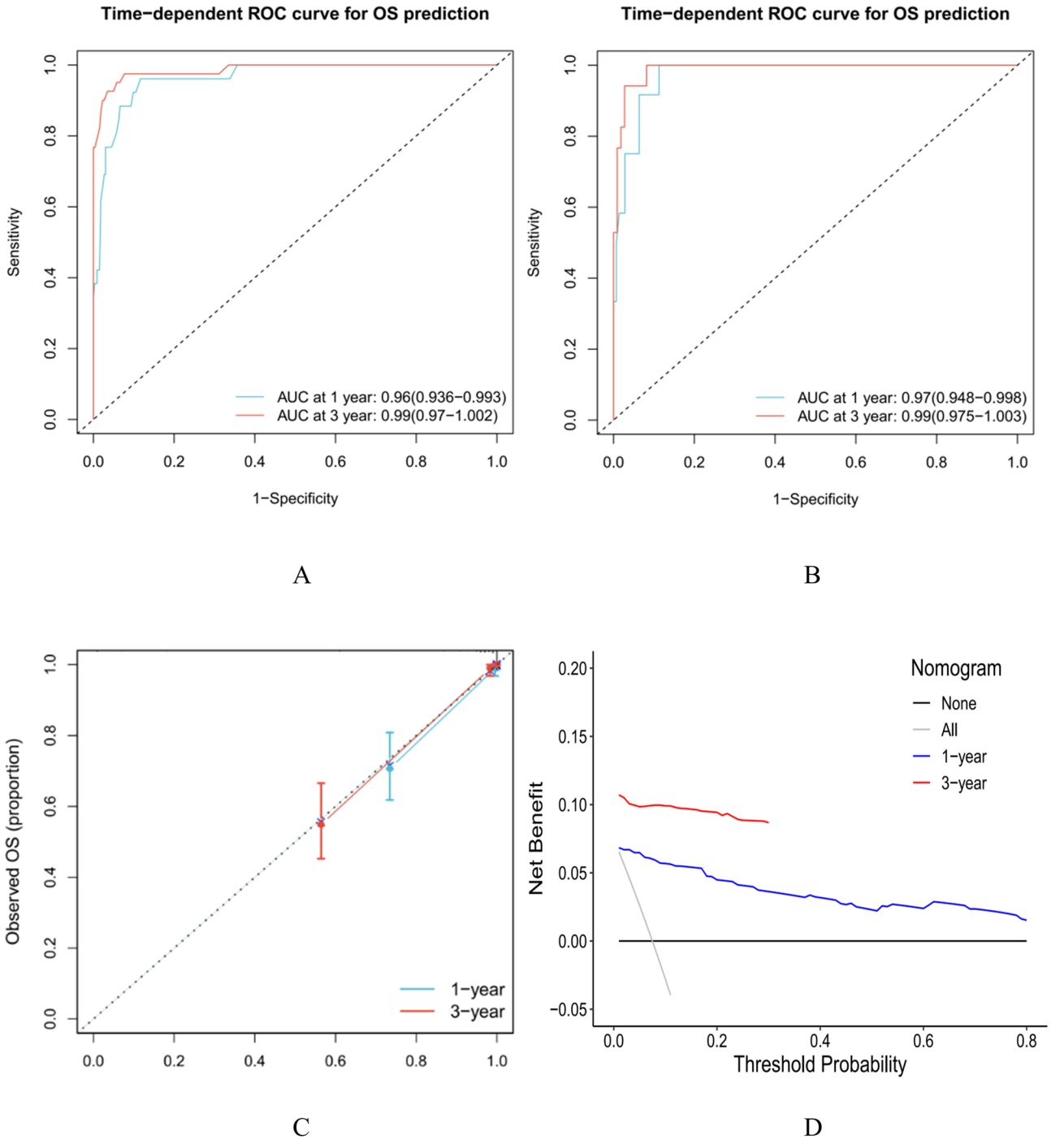

Fig. 3 **A**: ROC curve of the training set for a prediction model; **B**: ROC curve of the validation set for a prediction model; **C**: Calibration curve of the prediction model; **D**: DCA of 1-year and 3-year liver metastasis-free survival

risk factors for hepatic metastasis (surgical approach, N stage, degree of differentiation, vascular tumor thrombus, Lauren classification, P53 gene) through research and by referring to previous literature, but also achieves quantitative prediction of the risk of postoperative hepatic metastasis via a nomogram model, providing a new tool for clinical practice. Clinicians can identify high-risk patients based on the model results, thus optimizing follow-up strategies. For high-risk patients, it is recommended to appropriately increase the frequency of imaging examinations during follow-up, such as undergoing abdominal CT or MRI every three months, in order to detect potential liver metastases early. In addition, the model's predictive results can assist in the

development of individualized adjuvant treatment plans. For example, postoperative adjuvant chemotherapy or targeted therapy can be considered for high-risk patients to reduce the incidence of hepatic metastasis. However, it is important to avoid over-treatment and make careful decisions after weighing the benefits for patients against the costs of examinations. Future research should further verify the application value of the model in dynamic risk assessment to provide more precise guidance for clinical practice.

Limitations of the study

In exploring the risk factors for liver metastasis-free survival after surgery for AEG, although this study has achieved certain results, there are still some limitations that need to be overcome and improved in future research.

1. Limitations of a Single-Center Study: The data in this study were sourced from a single medical center, which may have introduced selection bias. To enhance the external validity of the research findings, future studies should adopt a multi-center study design to validate these findings in different populations.
2. Limitations of Retrospective Study Design: This study employed a retrospective study design, which cannot completely exclude the influence of confounding factors. Future research should use a prospective study design to better control for confounding factors.
3. Lack of External Validation: The results of this study have not been validated in an external independent dataset. Future research should undergo validation in other independent studies to enhance the reliability and generalizability of the research findings. However, due to the geographical concentration of adenocarcinoma of the esophagogastric junction in northern Henan Province, China, such as in Anyang City, the number of cases in hospitals in other regions of China is relatively low. As a result, external validation of this study is currently lacking. Future research will focus on collecting cases from other regions of China to address this limitation.
4. Siewert or Nishi classification data were not provided. During the study period, preoperative evaluations were indeed conducted for the enrolled patients according to the Siewert or Nishi classification. However, due to the long time, changes in the research team members, and the data preservation methods at that time, etc., the detailed Siewert or Nishi classification data that we have and are available for statistical analysis are very limited. These limited existing data are far from sufficient to represent the true distribution of the entire research cohort. Considering that such a small and incomplete amount of data may mislead readers and cannot objectively reflect the actual composition of the study population, we believe that the specific number of patients classified according to Siewert or Nishi in this article cannot be provided at present. We admit that the inability to provide the distribution of patients classified according to Siewert or Nishi is a limitation of this study. In future research, we will draw on this experience to further strengthen the standardized collection and management of clinical data and ensure the integrity of key information.
5. This study didn't cover the specific number of patients related to the tumor marker AFP and postoperative adjuvant chemotherapy. It's a retrospective study with a large sample size. In reality, it's impractical to recall patients for repeated AFP tests. Only a small number of patients in this study underwent AFP testing. Follow - up showed that for economic reasons, most patients didn't have the test. The limited number of cases made data analysis impossible. It should be noted that this study included patients with tumors of various stages and types. Nearly half of the patients didn't need postoperative adjuvant chemotherapy, or their families rejected it due to financial difficulties. Even among those who received chemotherapy, the treatment plans and cycles varied because of personalized treatment methods. So, this study didn't include the specific number of patients related to the tumor marker AFP and postoperative adjuvant chemotherapy. Expanding research collaboration in future studies may help to overcome the issue of insufficient single-center sample sizes in certain specific subgroups (such as patients receiving specific chemotherapy regimens or with specific markers). Through these improvements, future studies will be able to more comprehensively evaluate the specific roles of tumor markers and adjuvant therapy in patient prognosis.

Conclusion

Surgical approach, N stage, degree of differentiation, vascular tumor thrombus, Lauren classification, and P53 status are independent factors influencing liver metastasis-free survival after surgery for AEG. Based on these six factors, the constructed nomogram model for predicting liver metastasis after surgery for AEG demonstrates good predictive performance, at least in the areas like northern Henan in China.

Author contributions
DLL, SJ, and WJ were responsible for data collection and manuscript writing, while DXK and LBZ were responsible for reviewing the scientific accuracy of the manuscript.

Funding
Zhengzhou Municipal Science and Technology Innovation Guidance Plan Project in the Field of Medical and Health in 2024(No.2024YLZDJH107).
2024 Henan Province Medical Education Research Project (No: WJLX2024005).

Data availability
If you require the raw data, please contact the corresponding author at a2558040221@163.com.

Declarations

Ethics approval and consent to participate
This study was approved by the Hospital's Medical Ethics Committee (2024–069). It followed the principles of the Declaration of Helsinki. Written informed consent was obtained from all participants or their guardians.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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Received: 27 February 2025 / Accepted: 20 May 2025
Published online: 27 May 2025

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