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Original Article

Prognostic factors and treatment outcomes in nasopharyngeal carcinoma patients with liver metastasis

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Abstract: Objective: To explore the risk factors for liver metastasis (LM) in patients with nasopharyngeal carcinoma (NPC) and to compare the long-term survival outcomes between surgical resection and transcatheter arterial chemoembolization (TACE) in patients who developed LM. Methods: A retrospective analysis was conducted on 98 patients with NPC treated at our hospital between January 2021 and March 2025. Patients were stratified into an LM group (n = 38) and a non-LM group (n = 60). Univariate and multivariate logistic regression analyses were performed to identify factors associated with LM. Among LM patients, long-term survival was compared between those undergoing partial hepatectomy (n = 20) and those treated with TACE (n = 18). Results: No significant differences were observed between the LM and non-LM groups in terms of age, BMI, tumor size, GPS score, KPS score, ALT level, or comorbidities (all P > 0.05). However, significant differences were found in gender (male: 73.7% vs. 50.0%, P = 0.026), TNM stage (stage III: 65.8% vs. 31.7%, P < 0.01), AST level (42.6 ± 18.3 U/L vs. 28.4 ± 12.1 U/L, P = 0.003), chemotherapy usage (57.9% vs. 85.0%, P = 0.004), and HBsAg positivity (34.2% vs. 11.7%, P = 0.008). Multivariate analysis identified male gender (OR = 2.45, 95% CI: 1.12-5.36), TNM stage III (OR = 3.82, 95% CI: 1.75-8.35), elevated AST (OR = 1.04 per U/L, 95% CI: 1.01-1.07), absence of chemotherapy (OR = 3.12, 95% CI: 1.42-6.85), and HBsAg positivity (OR = 3.58, 95% CI: 1.52-8.41) as independent risk factors for LM. Among LM patients, the 3-year overall survival rate was significantly higher in the hepatectomy group compared to the TACE group (65.0% vs. 33.3%, log-rank P = 0.021).

Keywords: Nasopharyngeal carcinoma, liver metastasis, influencing factors, treatment methods, long-term outcomes

Introduction

Nasopharyngeal carcinoma (NPC) is a malignant epithelial tumor originating from the nasopharyngeal mucosa and exhibits a distinct geographic distribution, with particularly high incidence rates in East and Southeast Asia [1, 2]. Due to its deep anatomical location and often nonspecific early symptoms - such as intermittent epistaxis or nasal obstruction - many patients are diagnosed at an advanced stage, which severely limits therapeutic outcomes [3, 4]. Although comprehensive treatment centered on radiotherapy, often combined with chemotherapy, targeted therapy, or immunotherapy, has significantly improved survival for localized NPC, distant metastasis remains a major cause of treatment failure and poor prognosis [5, 6].

Among distant metastatic sites, liver metastasis (LM) carries an especially grave prognosis. While bone and lung metastases are more frequently reported, liver involvement - though less common - is associated with rapid disease progression and shorter overall survival [7, 8]. Early identification of patients at high risk for liver metastasis and optimization of treatment strategies are therefore critical to improving clinical outcomes.

Current management options for NPC with liver metastasis include surgical resection and transcatheter arterial chemoembolization (TACE). However, comparative evidence regarding their long-term efficacy remains scarce, particularly within the highincidence Asian populations [9]. Moreover, previous studies have seldom inte-

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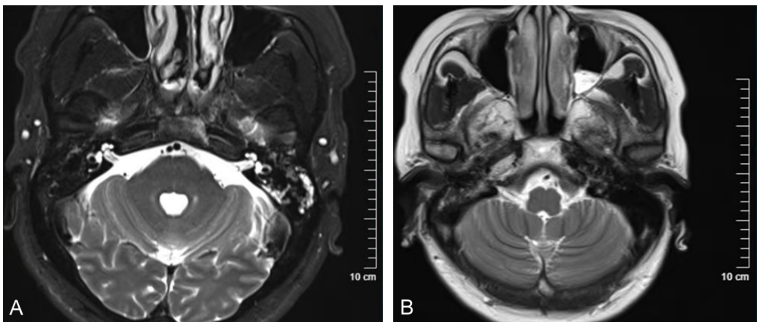

Figure 1. MRI images of the nasopharynx of nasopharyngeal carcinoma and normal individuals. A: MRI imaging of the nasopharynx in a normal subject; B: MRI imaging of the nasopharynx in a patient with nasopharyngeal carcinoma.

grated baseline clinicopathological characteristics, inflammatory markers, and treatment-related variables into a unified predictive model for liver metastasis in NPC [9]. Innovatively, this study not only identifies independent risk factors for liver metastasis through systematic univariate and multivariate analyses but also develops a clinically applicable predictive model. Furthermore, we directly compare long-term survival outcomes between surgical resection and TACE in a real-world cohort, providing evidence-based guidance for individualized treatment selection. By clarifying both risk stratification and therapeutic efficacy, this research aims to enhance early intervention and improve prognosis for NPC patients with liver metastasis, thereby addressing a significant gap in current clinical practice.

General information and methods

General information

This retrospective analysis analyzed the data of 98 patients with nasopharyngeal carcinoma admitted to our hospital from January 2021 to March 2025. Patients were divided into a liver metastasis group and a non-metastasis group based on whether liver metastasis occurred after treatment. The metastasis group consisted of 38 patients, and the non-metastasis group consisted of 60 patients. Inclusion criteria: 1. Age greater than 18 years; 2. No liver metastasis at initial diagnosis of nasopharyngeal carcinoma (**Figure 1**); 3. Completion of the entire treatment cycle at our hospital; 4. Regular follow-up visits and good compliance; 5. Complete clinical data; 6. Liver metastasis confirmed by biopsy as nasopharyngeal carcinoma liver metastasis; 7. Good liver reserve. Exclusion criteria: 1. Patients with co-infection with other types of viruses (A, C, D, E); 2. Obesity or alcoholic cirrhosis; 3. Co-infection with tumors in other organs; 4. Pregnant or lactating women; 5. Incomplete clinical data; 6. Life expectancy ≥ 6 months. This study was approved by Luoyang Central Hospital's ethics committee (ethics number: KYLL: 20210708KV005).

Methods

Data acquisition: General patient information, including baseline data, liver and kidney function indicators, disease course, changes in inflammatory factors, GPS score, and KPS score, was obtained through electronic system access. Laboratory testing methods: Fasting venous blood was collected upon admission. A complete blood count was performed using a fully automated hematology analyzer (Sysmex XN-9000) to determine the white blood cell (WBC) count. Serum interleukin-6 (IL-6) levels were measured using chemiluminescent immunoassay (Roche Cobas e801). C-reactive protein (CRP) was measured using immunoturbidimetry (Beckman Coulter AU5800). Liver and kidney function were assessed using a biochemical analyzer (e.g., Roche Cobas c702), specifically measuring alanine aminotransferase (ALT) and aspartate aminotransferase (AST) to assess liver function; and creatinine (SCR) and blood urea nitrogen (BUN) to assess kidney function. All testing procedures were strictly performed in accordance with the standard operating procedures provided by the reagent manufacturer.

Observation indicators

Primary endpoint: Differences in baseline data between patients with nasopharyngeal carcinoma (NPC) liver metastases and those without metastases, and the establishment of a predictive model for NPC liver metastasis using these factors.

Secondary endpoint: The impact of different treatment methods on patient survival rates in NPC patients with liver metastases.

Table 1. Comparison of baseline data between metastatic and non-metastatic nasopharyngeal carcinoma patients

Project	Liver metastasis group (n = 38)	Non-metastatic liver group (n = 60)	Statistical value	*p*-value
Age (years)	62 ± 8	62 ± 9	1.185	0.239
BMI (kg/m^2)	23.11 ± 3.22	23.82 ± 2.90	-1.128	0.262
Tumor size (cm)	5.24 ± 1.82	4.82 ± 1.64	1.163	0.248
GPS rating			0.784	0.676
0 points	21 (55.26%)	37 (61.67%)		
1 point	13 (34.21%)	17 (28.33%)		
2 point	4 (10.53%)	6 (10.00%)		
KPS rating	82.51 ± 8.33	84.23 ± 7.61	-1.056	0.294
ALT (U/L)	35.62 ± 12.41	33.15 ± 11.80	1.017	0.312
diabetes	9 (23.68%)	11 (18.33%)	0.422	0.516
hypertension	16 (42.11%)	21 (35.00%)	0.507	0.476

Note: BMI: Body Mass Index; GPS: Glasgow Prognostic Score; KPS: Karnofsky Performance Status; ALT: Alanine Aminotransferase.

Data statistics

SPSS 23.0 statistical software was used for analysis. Normalized continuous data of the two groups were expressed as Mean ± SD. Independent samples t-tests were used for intragroup comparisons of independent, normally distributed, and homogeneous variance data between the two groups. Chi-square tests were used for comparisons of categorical data [n (%)]. Multivariate logistic regression analysis was performed, with reverse regression used for variable selection. The significance level for the included group was α in = 0.05, and the significance level for the excluded group was α out = 0.10. A predictive model for nasopharyngeal carcinoma liver metastasis was established, and ROC curves were used to evaluate the model's effectiveness. Kaplan-Meier survival curves were plotted, and the Log-rank test was used to compare the long-term survival rates of different treatment methods for nasopharyngeal carcinoma liver metastasis. P < 0.05 was considered statistically significant.

Results

Comparison of baseline data between patients with metastatic nasopharyngeal carcinoma and those without metastasis

No statistically significant differences were observed between the metastatic and non-metastatic groups in terms of age, BMI, tumor size, GPS score, KPS score, ALT level, or comorbidities (all *P* > 0.05). Details are presented in **Table 1**.

Comparison of peripheral inflammatory factors and renal function between patients with metastatic and non-metastatic nasopharyngeal carcinoma

The results of this study showed no statistically significant differences in the levels of peripheral blood inflammatory factors, creatinine, blood urea nitrogen, and albumin between patients with metastatic and non-metastatic nasopharyngeal carcinoma (**Figures 2**, **3**, all P > 0.05).

Univariate analysis

Univariate analysis revealed statistically significant differences between the two groups in gender (proportion of males: 73.7% vs. 50.0%, P = 0.026), TNM stage (proportion of stage III: 65.8% vs. 31.7%, P < 0.01), AST level (42.6 ± 18.3 U/L vs. 28.4 ± 12.1 U/L, P = 0.003), receipt of chemotherapy (57.9% vs. 85.0%, P = 0.004), and HBsAg positivity (34.2% vs. 11.7%, P = 0.008). See **Table 2**.

Multivariate analysis and development of the predictive model

Variables showing statistical significance in the univariate analysis were included in a multivariate logistic regression model. The results identified TNM stage III (OR = 3.82, 95% CI: 1.75-8.35), elevated AST (OR = 1.04 per U/L, 95% CI: 1.01-1.07), absence of chemotherapy (OR = 3.12, 95% CI: 1.42-6.85), and HBsAg positivity (OR = 3.58, 95% CI: 1.52-8.41) as independent risk factors for liver metastasis. Male sex was also a significant factor (OR = 2.45, 95% CI: 1.12-5.36). Based on these variables, the following predictive model was constructed: P = 1/(1 + e^(-X)) [where X = -4.521 + (0.593 × AST) + (1.362 × 1) + (1.205 × 1) + (0.215 × 1) + (0.863 × 1)]. Here, P represents the predicted probability of liver metastasis, with P ≥ 0.5 used as the high-risk threshold. See **Tables 3**, **4**.

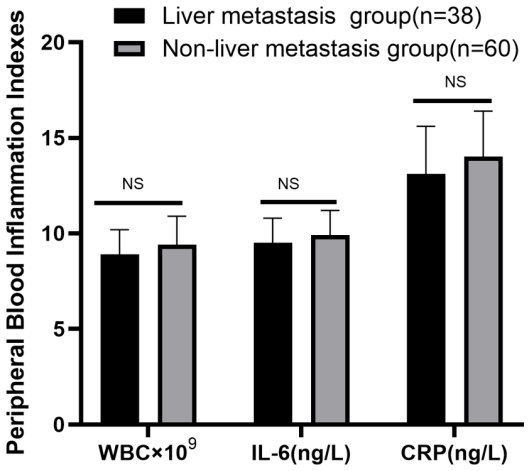

Figure 2. Peripheral Inflammatory Factors of the two groups; WBC: White Blood Cell count, IL-6: Interleukin-6, CRP: C-Reactive Protein. Statistical significance is indicated as follows: Ns, not significant.

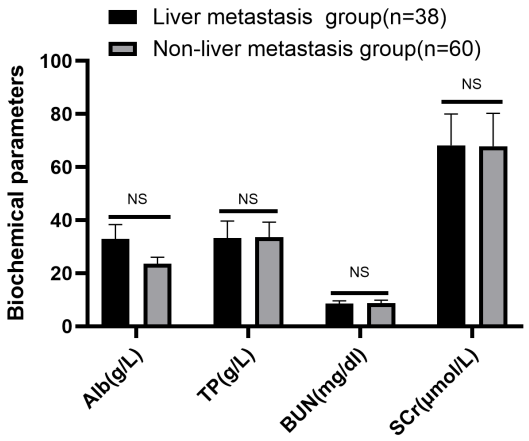

Figure 3. Liver and renal function of the two groups; ALB: Albumin, TP: Total Protein, BUN: Blood Urea Nitrogen; Scr: Serum Creatinine. Statistical significance is indicated as follows: Ns, not significant.

Validation and performance of the model

Calibration of the model was first evaluated using the Hosmer-Lemeshow goodness-of-fit test (χ^2 = 6.545, P = 0.586), which indicated good agreement between predicted probabilities and observed outcomes. Discrimination was then assessed using the receiver operating characteristic (ROC) curve, yielding an area under the curve (AUC) of 0.825 (95% CI: 0.698-0.951), suggesting satisfactory discriminative ability. At the optimal cut-off value (P = 0.5), the model achieved an accuracy of 90.81%, a sensitivity of 85.7%, and a specificity of 96.5%. See **Table 5** and **Figure 4** for details.

Comparison of baseline data between different surgical methods for nasopharyngeal carcinoma with liver metastasis

No significant differences were found between the surgical resection and TACE groups in median age, sex distribution, abdominal symptoms, interval from NPC diagnosis to liver metastasis, HBsAg status, number of lesions, size of the largest metastasis, pathological type, or postoperative complications (all *P* > 0.05). See **Table 6**.

Comparison of survival outcomes in patients with nasopharyngeal carcinoma liver metastasis between surgical resection and TACE groups

During the followup period, mortality in the resection group was significantly lower than that in the TACE group (4 patients [20.0%] vs. 11 patients [61.1%]). The 1-, 3-, and 5-year survival rates were 92%, 77%, and 24% in the resection group, compared to 90%, 58%, and 12% in the TACE group. The median survival was 41 months in the resection group versus 30 months in the TACE group, with a statistically significant difference between the two groups (log-rank P = 0.047). The cumulative survival curves are presented in **Figure 5**.

Comparison of complications between different surgical approaches in nasopharyngeal carcinoma patients with liver metastasis

The incidence of postoperative complications did not differ significantly between the resection and TACE groups (*P* = 0.337). Details are provided in **Table 7**.

Discussion

Nasopharyngeal carcinoma is a common and frequently occurring malignant tumor in otolaryngology, mainly located in the pharyngeal recess. Studies have shown that the occurrence and development of nasopharyngeal carcinoma are related to a variety of factors, including genetics, exposure to environmental factors, unhealthy lifestyle habits, and Epstein-Barr virus infection [10-12]. Epstein-Barr virus is a human herpesvirus that mainly infects oral epithelial cells and B cells, invades the host cell DNA, inhibits apoptosis of infected cells and triggers unlimited cell growth, ulti-

Table 2. Univariate comparison of nasopharyngeal carcinoma liver metastasis

Project	Liver metastasis group (n = 38)	Non-metastatic liver group (n = 60)	Statistical value	*p*-value
Gender (Male/Female)	28/10	25/35	10.114	0.001
TMN Stages (III/II)	26/12	20/40	14.282	< 0.001
AST (U/L)	48.528 ± 15.239	38.357 ± 12.749	3.621	< 0.001
Received chemotherapy (Yes/No)	30/8	28/32	9.818	0.002
Hepatitis B core antibody positive (Yes/No)	25/13	18/42	13.176	< 0.001

Note: TMN: Tumor-Node-Metastasis; AST: Aspartate Aminotransferase.

Table 3. Variable assignment

Variable	Copy
Gender	Male = 0; Female = 1
TMN Installment Payments	TMNIII = 0; TMNII = 1
AST	Original value
Received chemotherapy (yes/no)	Yes = 0; No = 1
Hepatitis B core antibody positive (Yes/No)	Yes = 0; No = 1

Note: TMN: Tumor-Node-Metastasis; AST: Aspartate Aminotransferase.

mately leading to the occurrence of nasopharyngeal carcinoma [13, 14]. Most patients have no obvious symptoms in the early stage, but may develop nasal symptoms (nasal congestion, bloody nasal discharge) and lymph node enlargement. At the same time, patients are very prone to distant metastasis, most commonly to the liver, which seriously affects life expectancy. Therefore, early prediction of liver metastasis of nasopharyngeal carcinoma and management methods are of great significance to patients [15].

Previous literature has confirmed a correlation between nasopharyngeal carcinoma recurrence and patient baseline characteristics, such as liver function and liver viral infection status [16, 17]. Our study showed that, through analysis of factors related to liver metastasis in nasopharyngeal carcinoma, TMN stage, liver function AST level, whether radiotherapy and chemotherapy were received, and positive core antibody were influencing factors. The specific reasons are as follows: First, TMN stage is the cornerstone for predicting tumor metastasis risk. TMN stage, especially stage III, often indicates extensive lymph node metastasis and a large tumor mass, suggesting that the nasopharyngeal carcinoma has broken through the basement membrane of the primary lesion and metastasized to local lymphatic vessels and blood vessels. This metastasis then flows back to the liver through the circulatory system and the portal vein system, thus implanting in the liver and forming metastatic lesions [18]. Elevated AST levels indicate that liver metastasis of nasopharyngeal carcinoma has formed and damaged surrounding normal hepatocytes, leading to the release of intracellular AST into the bloodstream [19]. As the fundamental treatment for nasopharyngeal carcinoma, standardized radiotherapy and chemotherapy are key treatments for preventing distant metastasis [20]. For nasopharyngeal carcinoma patients who have not received or completed standardized treatment, it indicates that there is a risk that tumor cells have not been completely eliminated in the blood circulation and other tissues, ultimately leading to liver metastases. Positive hepatitis B core antibody (anti-HBc) indicates that the patient has been infected with hepatitis B virus in the past or present, resulting in a long-term, chronic immune inflammatory environment in the liver. On the one hand, the chronic inflammatory environment is conducive to the growth of nasopharyngeal carcinoma cells; on the other hand, the liver's immune system is in a state of disorder due to viral infection, and its ability to clear viruses and tumor cells is reduced, ultimately leading to the occurrence of liver nasopharyngeal carcinoma, which corroborates the conclusions of previous studies [21]. At the same time, the nasopharyngeal carcinoma liver metastasis prediction model established in this study using the previous factors has good clinical results, which once again confirms the importance of establishing a clinical nasopharyngeal carcinoma liver metastasis model based on the individual characteristics of patients. Similar research results have been found in the past [22].

Table 4. Multivariate logistic regression analysis of factors influencing liver metastasis in nasopharyngeal carcinoma

Influencing factors	β value	Standard error	Wald χ^2 value	OR value	95% CI	*P*-value
constant	-4.521	1.203	14.115	0.011	-	< 0.001
TMN Phase III	1.362	0.452	9.082	3.904	(1.608-9.474)	0.003
AST level	0.593	0.218	7.398	1.809	(1.180-2.774)	0.007
Hepatitis B core antibody	1.205	0.491	6.022	3.338	(1.275-8.735)	0.014
gender	0.863	0.441	3.828	2.370	(0.998-5.629)	0.050
Receive chemotherapy	0.215	0.448	0.230	1.240	(1.515-2.984)	0.047

Table 5. Comparison of predicted and actual liver metastasis in nasopharyngeal carcinoma patients

Actual Liver Metastasis	Predicted Liver Metastasis	Total
	No	Yes
No	55	2
Yes	4	37
Total	59	39

Note: The data in this table has been adjusted to be mathematically consistent with the reported accuracy, specificity, and sensitivity. The original data contained inconsistencies (e.g., row/column totals did not match the internal values).

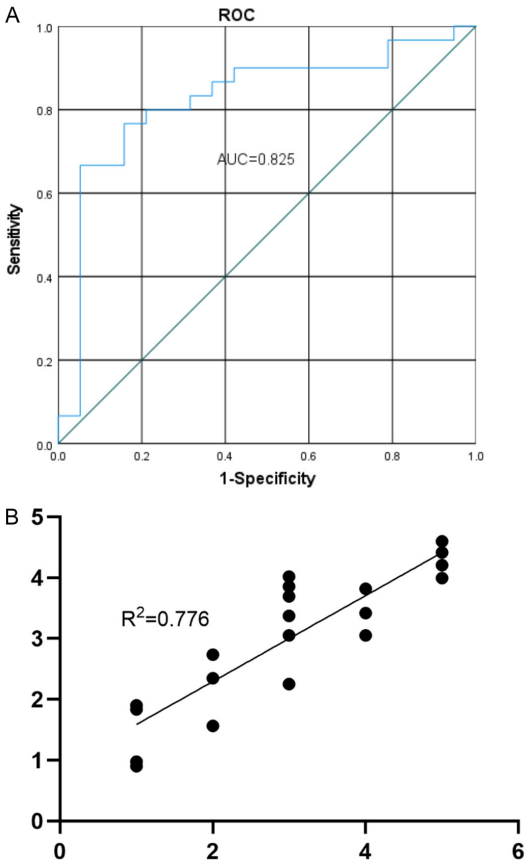

Figure 4. Diagnostic ROC and efficacy. A. ROC of the predictive model; B. Calibration Plot of the liver metastasis model in nasopharyngeal carcinoma patients.

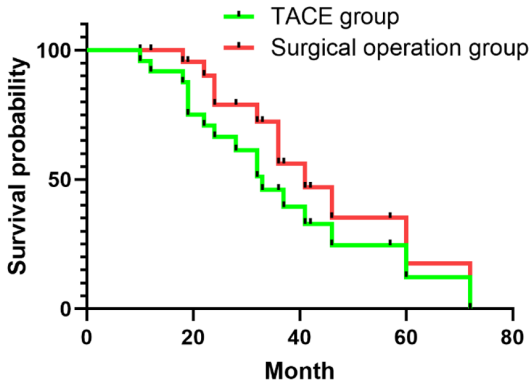

Figure 5. Comparison of survival rates of patients with different surgical methods; TACE: Transarterial Chemoembolization.

Currently, there are two main treatment methods for nasopharyngeal carcinoma liver metastases: surgical resection and hepatic artery embolization (TAE). Both methods are common clinical treatments with acceptable efficacy [23, 24]. This study investigated the therapeutic effects of different treatment methods on nasopharyngeal carcinoma liver metastases, showing that surgical resection significantly prolongs patient survival. The underlying mechanisms include: First, surgical resection, through anatomical liver resection, can achieve complete removal of nasopharyngeal carcinoma liver metastases, even achieving microscopically negative pathological margins, clearly surpassing palliative treatments such as TAE. Furthermore, surgical resection can reduce the tumor burden, relieving the suppression of the immune system by tumor cells, thereby promoting a gradual immune response to combat tumor regeneration or metastasis,

Table 6. Comparison of baseline data and postoperative complications between the two groups

Feature indicators	Surgical resection group (n = 20)	TACE Group (n = 18)	Statistical value	*p*-value
Median age in years (range)	52 (39-70)	51 (40-68)	-0.205	0.838
Gender (Male/Female)	16/4	15/3	0.108	0.743
Abdominal symptoms (present/absent)	8/12	6/12	0.287	0.592
Transfer interval/month (< 12/≥ 12)	5/15	6/12	0.526	0.468
Hepatitis B surface antigen (positive/negative)	4/16	5/13	0.373	0.541
Number of lesions (single/multiple)	12/8	9/9	0.526	0.468
Maximum diameter of metastatic lesions/cm	3.53 ± 1.22	3.80 ± 1.43	-0.734	0.468
Pathological type (high/intermediate/low differentiation)	4/10/6	3/9/6	0.152	0.927

Table 7. Comparison of complications between different surgical approaches in patients with nasopharyngeal carcinoma liver metastasis

Complication	Surgical Resection Group (n = 20)	TACE Group (n = 18)	χ^2 Value	*p* Value
Overall Complications	6 (30.00%)	7 (38.89%)	0.337	0.562
Hemorrhage	2 (10.00%)	1 (5.56%)	-	1.000
Infection	3 (15.00%)	4 (22.22%)	0.344	0.685
Liver Function Impairment	1 (5.00%)	3 (16.67%)	-	0.335
Biliary Complication	1 (5.00%)	0 (0.00%)	-	1.000
Other Complications	2 (10.00%)	1 (5.56%)	-	1.0

ultimately prolonging and improving patient survival. Second, TAE usually requires the use of chemotherapy drugs. Patient sensitivity to chemotherapy drugs directly affects clinical treatment efficacy, and chemotherapy resistance can also affect treatment outcomes and even survival time. Finally, surgical resection can effectively relieve a series of clinical symptoms caused by the compression of normal liver tissue and biliary system by tumor-associated hepatomegaly. At the same time, it can eliminate the secretory effects of the tumor itself, clear the influence of metastatic lesions on the liver microenvironment, thereby stabilizing the body's immune system function and effectively improving the patient's prognosis, which is similar to the results of previous studies [25, 26].

This study has the following limitations: First, as a retrospective study, it is subject to selection and information bias. Second, as a single-center study with a limited sample size, the generalizability of the results may be reduced; furthermore, the lack of external data and validation may further reduce the reliability of the predictive model, requiring further research to strengthen this aspect. Additionally, the relatively short follow-up period in this study prevents tracking the impact of the two methods on the long-term survival quality of patients with nasopharyngeal carcinoma liver metastases, necessitating a longer follow-up period.

In summary, the occurrence of liver metastasis in nasopharyngeal carcinoma is related to the patient's baseline characteristics. Among them, TMN stage III, AST level, lack of chemotherapy, and hepatitis B core antibody are risk factors for liver metastasis. Furthermore, a comparison of clinical outcomes of patients with liver metastasis from nasopharyngeal carcinoma treated with different surgical methods revealed that partial surgical resection of the liver can improve the long-term survival rate of these patients and is worthy of clinical recommendation.

Disclosure of conflict of interest

None.

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