Risk factors to predict ocular metastasis in older adult patients with gastric cancer:LDL, ApoA1, and CA724

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Research

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Abstract

Background: Gastric cancer (GC) is one of the most common malignancies in the population. Although the incidence of GC has reduced, patient prognosis remains poor. Ocular metastases (OM) from GC are rare, and the occurrence of OM is often indicative of severe disease. The purpose of this study was to explore the risk factors for OM of GC.

Methods: A total of 1165 older adult patients with GC were enrolled in this study from June 2003 to May 2019 and divided into OM and non-ocular metastasis (NOM) groups. Chi-square and independent samples *t* tests were used to determine whether differences in demographic characteristics and serological indicators (SI) between the two groups were significant. In addition, binary logistic regression was used to analyze the value of various SI as risk factors for OM in patients with GC. The statistical threshold was set as $P < 0.05$. Finally, receiver operating characteristic (ROC) curve analysis was used to assess the diagnostic value of various SI in differentiating the occurrence of OM in patients with GC.

Results: The incidence of OM in older adults with GC was 1.1%. Adenocarcinoma was the most common type of GC in both groups, and there was no significant difference in demographic characteristics, including sex and age between the groups. Low-density lipoprotein (LDL), carbohydrate antigen-724 (CA724), and carcinoembryonic antigen levels were significantly higher in the OM group than the NOM group, while those of apolipoprotein A1 (ApoA1) were significantly lower in the OM than the NOM group. Binary logistic analysis showed that LDL, ApoA1, and CA724 were independent risk factors for OM in patients with GC ($P < 0.001$,$P = 0.033$, and $P = 0.008$, respectively). ROC curve analysis generated area under the curve (AUC) values of 0.881, 0.576, and 0.906 for LDL, ApoA1, and CA724, respectively. In addition, combined analysis of LDL, ApoA1, and CA724 generated the highest AUC value of 0.924 ($P < 0.001$).

Conclusion: Among SI, LDL, ApoA1, and CA724 have predictive value for the occurrence of OM in GC, with the three factors combined having the highest value.

Background

As the fourth most common malignant tumor worldwide, gastric cancer (GC) has a poor prognosis and a high mortality rate, representing the third leading cause of cancer-related death.[1] GC features a high degree of malignancy, rapid development, strong invasiveness, easy recurrence, and poor prognosis. Among these characteristics, invasion and metastasis are important malignant features of GC, and the main causes of death in patients with this disease.[2] A series of related studies of GC have shown that excessive salt intake, smoking, alcohol consumption, and *Helicobacter pylori* (*H. pylori*) infection are all risk factors for GC.[3] In recent years, dietary changes, improvements in hygiene, and awareness of health and nutrition have significantly reduced the incidence of GC in specific geographical regions. In contrast, the *H. pylori* infection rate has increased significantly, and the incidence of GC remains high. *H. pylori* infection can induce DNA methylation and histone modification in gastric epithelial cells, thus promoting

the development of GC.[4] Further, *H. pylori* promotes the invasion and metastasis of GC by enhancing heparinase expression.[5] In addition, epidemiological studies demonstrate that the incidence of GC in men is twice that in women in areas where there is a high risk of GC.[6]

The common GC pathological classification method is Lauren classification, which primarily divides GC into localized and diffuse categories.[7] GC can affect every aspect of a patient's life. Patients with early GC may have no obvious clinical symptoms; however, those with advanced GC may show significant weight loss, difficulty swallowing, abdominal pain, vomiting, and even severe upper gastrointestinal bleeding. At present, treatment of GC often involves surgical resection of the tumor, radiotherapy, and chemotherapy. Radiotherapy and chemotherapy are often used to treat patients with advanced GC who cannot tolerate surgery or for whom surgery will be of relatively little value, and can improve the overall survival rate of patients to some extent; however, cancer recurrence or metastasis is often reported.

Exosomes, an important group of extracellular vesicles, have important roles in the initiation, progression, and metastasis of GC.[8] Lymph node metastasis is the main route of metastasis in the process of tumor migration. Most patients diagnosed with GC have lymph node metastasis; even in early GC, the proportion of patients with lymph node metastasis is 5.7%–29.0%.[9] In addition to lymphatic metastasis, other common metastasis pathways of GC include direct invasion, hematogenous metastasis, and peritoneal implantation metastasis. Common sites of GC metastases include the peritoneum, liver, spleen, lung, and lymph nodes;[10] however, the number of cases of ocular metastasis (OM) in GC is very small. One study reported metastasis of GC in the extraocular muscle;[11] in this case, the patient presented with poorly differentiated adenocarcinoma and the main ocular clinical manifestations were eyelid swelling, diplopia, and retroorbital pain. OM in patients with GC is often an indicator of poor prognosis, as the cancer cells may have metastasized to multiple sites throughout the body. Metastasis of GC is an independent prognostic risk factor for GC patients, and seriously influences treatment and prognosis.

The occurrence of OM in patients with GC has a great impact on their quality of life; however, the specific processes and mechanisms underlying of metastasis of primary GC remain unclear, despite frequently resulting in substantial patient suffering. The circular RNA, circUBA1, can promote GC proliferation and metastasis by regulating the effects of miR-375 and TEAD4;[12] however, this factor is seldom assessed in clinical practice, because of the technical difficulty and complexity of its method of measurement. Serological indictors (SI), as indicators routinely detected in clinical practice, have specific advantages for use in the diagnosis of GC metastasis, and can be important indicators for diagnosis of GC metastasis by the gold standard methods of auxiliary pathology. Cancer markers refer to substances produced directly by tumor cells or by non-tumor cells through tumor cell induction. The detection of tumor markers can predict the existence, pathogenesis, and prognosis of tumors.[13] In our study, we investigated whether changes in cancer biomarkers and SI can be used to differentially diagnose OM in patients with GC. In addition, by studying the correlations among various risk factors and the occurrence of OM in GC, we established a relatively accurate index to distinguish between patients with and without OM, to

facilitate possible diagnosis at an early stage of GC metastasis, conduct timely intervention, and further improve the prognosis and quality of life for patients with GC.

Methods

Study design

This retrospective study was approved by the Medical Research Ethics Committee of the First Affiliated Hospital of Nanchang University. The study included older adult patients (age ≥ 60 years) diagnosed with GC between June 6, 2003 and May 15, 2019. A total of 1165 patients with GC were recruited to this study. Patients with secondary GC were excluded. GC was confirmed in all patients by surgical resection and histopathological biopsy. Subjects were divided into OM and non-ocular metastasis (NOM) groups. The inclusion criteria for the OM group were eye metastases in patients with GC diagnosed by CT and MRI and confirmed by histology and cytology. Patients with primary eye tumors (benign or malignant) were excluded from the OM group. All subjects provided signed informed consent.

Data collection

Medical records of all participants were collected to acquire basic information about their age, sex, and pathological tumor type. In addition, serological data were collected from both groups of subjects, including: hemoglobin (HB), calcium, alkaline phosphatase (ALP), total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL), low-density lipoprotein (LDL), apolipoprotein A1 (ApoA1), apolipoprotein B (ApoB), alpha fetoprotein (AFP), carbohydrate antigen-724 (CA724), carcinoembryonic antigen (CEA), CA199, CA125, CA153, cytokeratin-19 fragment (CYFRA21-1), and lipoprotein(a) (Lp(a)) levels.

Statistical analyses

The chi-square test was used to compare the sex distribution and pathological types between the OM and NOM groups. A two-tailed independent sample t-test was used to assess differences in age and levels of various SI between the two groups. A binary logistic regression model was used to analyze the significance of the associations of various SI with OM in older adult patients with GC. Finally, receiver operating characteristic (ROC) curves were used to analyze the significance of each indictor in differentiating OM and NOM. The statistical threshold used was $P < 0.05$. SPSS 25.0 (IBM, USA) and Excel 2019 (Microsoft Corporation, USA) software were used for data analyses.

Results

Demographic and clinical characteristics of participants

The total number of GC patients enrolled in this study was 1165, including 13 in the OM group and 1152 in the NOM group, with 1.1% of patients with GC diagnosed with OM. The mean age of patients in the OM group was 67.9 ± 6.5 years, while that in the NOM group was 68.3 ± 15.7 years ($P > 0.05$, *t*-test). There

were no significant differences in sex distribution or tumor pathological type between the two groups (P > 0.05, chi-square test); the ratio of males to females was 2.53:1, and the pathological type in both groups was mainly gastric adenocarcinoma. The results of fundus examination and related histopathological tests, and patient clinical information are detailed in Table 1 and Figure 1–3.

Differences in the levels of various serological indicators and risk factors between the two groups

Compared with the NOM group, among all SI, LDL, CA724, and CEA levels were significantly higher in the OM group, while those of ApoA1 were significantly lower (P < 0.05). Levels of other SI, including HB, calcium, ALP, TC, TG, HDL, ApoB, AFP, CA199, CA125, CA153, CYFRA21-1, and Lp(a), did not differ significantly between the two groups (P > 0.05). Furthermore, according to binary logistic regression analysis, LDL, ApoA1, and CA724 were independent risk factors for OM. More detailed data are presented in Table 2 and Table 3.

ROC analysis to determine the value of LDL, ApoA1, and CA724 for diagnosis of OM

Through ROC analysis, we determined cut-off values for LDL, ApoA1, and CA724 of 3.98 mmol/L, 1.71 g/L, and 14.08 U/mL, respectively; CA724 had the highest AUC value. ROC curves to assess each indicator as a risk factor for OM in patients with GC are shown in Figure 4A. We also assessed the significance of the ratios of LDL to ApoA1 and CA724 to ApoA1, as well as various combinations of indicators, including: LDL+ApoA1, LDL+CA724, CA724+ApoA1, and LDL+ApoA1+CA724, as risk factor indicators for assessment of OM occurrence in patients with GC. Analysis of combined indicators demonstrated that LDL+ApoA1+CA724 had the highest AUC value (0.924). Further, the AUC value of LDL+CA724 was regimen also reached 0.918 (Figure 4B). Among the above indicators, the sensitivity of CA724, CA724/ApoA1, and CA724+ApoA1 was the highest, reaching 1, while the specificity of the combination of LDL+ApoA1 was the highest, at 0.94. All the above results were statistically significant (P < 0.05). Detailed data are presented in Table 4.

Discussion

In this study, we retrospectively analyzed data from 1165 patients with GC, and conducted a detailed study on pathological classification and risk factors for OM. A related study showed that the morbidity of GC is closely related to age, and that the age of onset is mainly concentrated in middle-aged and older adults, among which the latter have the highest incidence.[14] Here, we found that the ratio of male to female patients with GC was unbalanced at 2.53:1. Based on relevant publications, we infer that factors influencing the high incidence in males include continuous stimulation of the cerebral cortex because of work pressure and mental stress, continuous excitation of the sympathetic nerve, and subsequent induction of chronic atrophic gastritis, gastric ulcer, and other precancerous lesions.[15] Moreover, the high concentrations of estrogen in females inhibits the expression of estrogen receptor 36 (ER 36) and the growth of GC cells, which has protective effects on the stomach.[16] At present, known risk factors for GC are primarily irregular diet and *H. pylori* infection. Furthermore, genetic factors are an important cause of

GC.[17] First degree relatives of patients with GC have a higher risk of GC than the general population, with a clear tendency toward familial aggregation.[18] Among the participants in our study, gastric adenocarcinoma accounted for 94%, followed by the more malignant tumor, signet ring cell carcinoma (SRCC), which accounted for 4% of cases.

For patients with early GC, the risk of metastasis is relatively low, and those without metastasis can undergo submucosal dissection or tumor removal using endoscopic technology. [19] In clinical practice, patients with GC are often at an advanced stage of disease on definite diagnosis, and a considerable number develop distant metastasis of cancer cells. Cancer-associated fibroblasts (CAF), an important component of various tumors, are involved in the invasion and metastasis of GC.[20] Numerous researchers have studied the risk factors for GC metastasis, [21-27] and their findings are summarized in Table 5; however, there are few reports of OM of GC to date. Tadashi et al. reported a case of ptosis caused by orbital metastasis in a patient with advanced GC, diagnosed using CT and MRI technology, which are still widely used for clinical diagnosis of cancer metastasis.[28] In addition, another study reported a case of iris metastasis in a patient with GC undergoing chemotherapy. [29] In terms of clinical symptoms, iris metastasis of GC is relatively insidious, and easily misdiagnosed as iridocyclitis. During clinical diagnosis and treatment, full integration of the patient's medical history and the results of examinations is required to ensure accurate judgments; however, in current clinical practice, it remains difficult to accurately identify OM of GC at an early stage. Further, CT and MRI are expensive examination methods, and there can be contraindications to their use, leading to limited sensitivity and specificity. In contrast, serological tumor markers are widely used in clinical practice, due to their advantages of good reproducibility, low cost, and easy access. To date, a considerable number of researchers have proposed various serological markers related to disease metastasis and prognosis; however, there is a lack of specific SI for OM in older adult patients with GC. In our study, we collected serological data from 1165 patients with GC, including: HB, calcium, ALP, TC, TG, HDL, LDL, ApoA1, ApoB, AFP, CA724, CEA, CA199, CA125, CA153, CYFRA21-1, and Lp(a) and found that LDL, ApoA1, CA724, and CEA content differed significantly between the OM and NOM groups. Compared with the NOM group, LDL, CA724, and CEA levels were significantly higher in the OM group, while those of ApoA1 were significantly lower. In addition, LDL, ApoA1, and CA724 concentrations were independent risk factors applicable for differential diagnosis of OM by statistical analysis. Subsequently, we analyzed and determined the threshold values, sensitivity, specificity, and AUC values for each biomarker by constructing ROC curves, further confirming that LDL, ApoA1, and CA724 are important markers for OM in older adult patients with GC. Finally, we conclude that, at their respective thresholds of 3.98 mmol/L, 1.71 g/L, and 14.08 U/mL, LDL, ApoA1, and CA724 are indicators that patients with GC are at risk of developing OM. The ability to differentiate and diagnose OM could be further improved by combining changes in serological indicators with clinical imaging techniques, such as eye CT and MRI, to ensure timely treatment and improve patient prognosis.

LDL is a cholesterol-rich lipoprotein that carries cholesterol into peripheral tissue cells. Excess LDL is closely associated with atherosclerosis, myocardial infarction, stroke, and peripheral artery disease. In addition, study of a hyperlipidemia mouse model showed that LDL and tumor cell LDL receptor

expression can mediate the growth and recurrence of breast cancer.[30] Further, LDL and VLDL can promote the proliferation, differentiation, and metastasis of breast cancer cells.[31] Moreover, LDL levels are reportedly positively correlated with the occurrence of liver metastasis of colorectal cancer, and LDL can promote inflammatory responses in the gastrointestinal tract and colorectal cancer progression by activating signaling pathways, including ROS and MAPK pathways.[32] In a study to explore the relationship between lipid levels and the risk and prognosis of GC, patients with GC had significantly increased LDL content, consistent with our results.[33]

ApoA1 refers to the apolipoprotein attached to HDL and chylous glomeruli. ApoA1 plays an important role in physiological lipid metabolism, and is often regarded as a biomarker to predict the risk of coronary heart disease in individuals.[34] In a mouse MKN45 gastric cancer xenograft model, decreased plasma ApoA1 levels were closely associated with GC growth.[35] In addition, some prognostic studies of have demonstrated that the ApoB/ApoA1 ratio can be used as an independent prognostic factor for GC; the survival time of GC patients with ApoB/ApoA1 ratio ≥ 1 is significantly shortened.[36] Further, decreased ApoA1 levels have been associated with poor prognosis of patients with colorectal cancer and systemic inflammatory response.[37] In our study, the level of ApoA1 in the OM group was significantly lower than that in the NOM group, and the occurrence of OM in patients with GC often indicates poor prognosis, consistent with the conclusions of the above research.

As a GC antigen, CA724 is an important tumor marker for detection of GC and various gastrointestinal cancers. Due to its high sensitivity, CA724 is very commonly used as a clinical marker for detection of GC. In multivariate analysis based on the Chinese population, Chen et al. clearly demonstrated that, compared with other tumor markers, CA724 had the highest correlation with the occurrence of GC in the Chinese population. [38] Moreover, in a study of lymph node metastasis in patients with GC, lysyl oxidase, CEA, CA724, CA199, and CA125 were identified as significantly improving the sensitivity for detecting lymph node metastasis.[39] Monitoring alterations in CA724 concentration during chemotherapy in patients with advanced GC can be used as a predictor of tumor response.[40] In our study, we found that CA724 content in the OM group was higher than that in the NOM group. Based on our data, combined with previous reports, we conclude that patients in the OM group may have a relatively poor prognosis, since it is likely that many cancer cells have metastasized.

Finally, we tested combinations of LDL+ApoA1, LDL+CA724, ApoA1+CA724, and LDL+ApoA1+CA724, and the ratios of LDL to ApoA1 and CA724 and ApoA1, as indicators for ROC analysis, calculating AUC values for each combined indicator. LDL+ApoA1+CA724 generated the maximum AUC value, followed by LDL+CA724. Hence, these two combination indicators can more accurately predict the occurrence of OM in GC.

Our study has some limitations. First, it is a retrospective analysis; hence, there may be recall bias. Second, as eye metastasis of GC is very rare, only 13 cases of OM occurred among the 1156 patients with GC included our analysis. Further studies with larger sample sizes may provide more accurate

results. In addition, the data analyzed in our study did not include survival rates or follow-up findings, and specific patient prognoses were not analyzed. Finally, since all of our patients were from a single medical center, our results may not be representative of all populations with OM from GC.

Conclusions

In summary, risk factors for the occurrence of OM in GC include LDL, ApoA1, and CA724, and a combination of these three diagnostic indicators is most valuable for predicting the occurrence of OM in GC. Our research can assist in evaluation of the condition of patients over time, improve patient prognosis, and play a crucial role in the processes of disease screening, diagnosis, and treatment.

Abbreviations

OM：Ocular metastasis

NOM: Non-ocular metastasis

HE: Hematoxylin-eosin

IHC: Immunohistochemistry

SP: streptavidin-peroxidase

GC: Gastric cancer.

LDL: low-density lipoprotein

ApoA1: Apolipoprotein A1

CA724: Carbohydrate antigen-724

THBS4: Thrombospondin 4

CEA: Carcinoembryonic antigen

CA199: Carbohydrate antigen-199

ENO1: Alpha-enolase

HOXC10: homeobox C10.

Declarations

Ethics approval and consent to participate

Prior patient consent and institutional research ethics committee approval were obtained for the use of these clinical materials for research purposes.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Consent for publication

All authors read and consented to publication of the paper.

Competing interests

This was not an industry supported study. The authors report no conflicts of interest in this work.

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Authors' contributions

WQ, TS, and YS participated in the design and statistical analysis of this study. SW, HS, QY, and QL collected the data, and TS and YP reviewed the references. RL, YS, and SW drafted the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1 The clinical characteristics in OM group and NOM group.

Patient characteristics	OM Group[1] (n=13) (1.1%)	NOM Group (n=1152) (98.9%)	P value[4]
Gender[2]			0.298
Male	11	824	
Female	2	328	
Age[3]			
Mean	67.9±6.5	68.3±15.7	0.929
Histopathological type[2]			
Adenocarcinoma	12	1083	0.496
Signet ring cell carcinoma	1	50	
Squamous cell carcinomas	0	6	
Others	0	13	

P<0.05 indicates statistical significance.

[1]OM, including intraocular metastasis and eyelid metastasis.

[2]Chi-squared test.

[3]Student' s t test.

[4]Comparison between the OM and NOM groups.

Notes: Data showed as mean ± standard deviation or n.

Table 2 Differences in the concentration of various tumor biomarkers between OM and NOM.

Tumor biomarkers	OM group	NOM group	t-test	P-value
HB(g/L)	119.85±15.55	114.10±20.47	-1.008	0.314
Calcium (mmol/L)	2.27±0.22	2.64±8.89	0.152	0.879
ALP (U/L)	128.31±104.81	106.61±105.81	-0.735	0.462
TC(mmol/l)	4.83±1.51	4.72±1.57	-0.269	0.788
TG(mmol/L)	1.80±1.62	1.71±2.27	-0.141	0.888
HDL(mmol/L)	1.77±1.37	1.68±1.20	-0.283	0.777
LDL(mmol/L)	5.26±1.38	2.96±1.42	-5.802	0.000
ApoA1(g/L)	1.43±0.28	1.65±0.57	2.686	0.019
ApoB(g/L)	1.34±1.43	1.22±0.93	-0.443	0.658
AFP(ng/mL)	3.32±1.88	3.51±2.22	0.305	0.760
CEA(ng/mL)	15.67±10.18	6.02±10.39	-3.329	0.001
CA724 (U/mL)	16.47±2.66	7.57±9.59	-3.345	0.001
CA125 (U/mL)	52.96±111.21	41.12±77.80	-0.542	0.588
CA153 (U/mL)	11.72±7.69	15.31±15.53	0.834	0.405
CA199 (U/mL)	31.34±53.05	31.43±61.61	0.005	0.996
CYFRA21-1(ng/mL)	2.89±1.46	5.70±9.94	1.018	0.309
Lp(A)(mg/L)	261.92±168.16	213.87±158.39	-1.087	0.277

Notes: Independent sample t-test. P<0.05 denoted statistical significance. Data showed as mean ± standard deviation.

Abbreviation: OM, ocular metastasis; NOM, non-ocular metastasis.

Table 3 Risk factors of OM in elderly patients with GC.

Tumor marker	B	Exp(B)	OR (95% CI)	P Value
LDL	2.085	8.045	3.644-17.763	0.000
ApoA1	-2.333	0.097	0.011-0.827	0.033
CA724	0.059	1.061	1.016-1.108	0.008

Notes: Binary logistic regression analysis. P<0.05 denoted statistical significance.

Abbreviation: B, coefficient of regression; OR, odds ratio; CI, confidence interval; OM, ocular metastasis; GC, gastric cancer.

Table 4 The Cut-off Value, sensitivity, specificity, and AUC of risk factors for the prediction of OM in elderly GC patients.

Factor	Cut-Off Value	Sensitivity (%)	Specificity (%)	AUC	P value
LDL(mmol/L)	3.98	0.85	0.85	0.881	<0.001
ApoA1(g/L)	1.71	0.92	0.35	0.576	0.348
CA724(U/mL)	14.08	1.00	0.87	0.906	<0.001
LDL/ApoA1	2.61	0.92	0.82	0.906	<0.001
CA724/ApoA1	7.34	1.00	0.79	0.905	<0.001
LDL+ApoA1	-	0.77	0.94	0.892	<0.001
LDL+CA724	-	0.92	0.82	0.918	<0.001
CA724+ApoA1	-	1.00	0.81	0.896	<0.001
LDL+ApoA1+CA724	-	0.92	0.85	0.924	<0.001

Notes: Sensitivity and specificity were acquired at the cut-off value. $P < 0.05$ denoted statistical significance.

Abbreviations: AUC, area under the curve; OM, ocular metastasis; GC, gastric cancer.

Table 5 The risk factors of metastases of gastric cancer.

Author	Year	Metastatic Sites	Risk factor
Chen et al[21]	2019	NS	THBS4
Liu et al[22]	2015	Lymphoid node	Claudin-4
Jing et al[23]	2020	Lymphoid node	CEA, CA199
Ji et al[24]	2019	NS	LINC00086, miR-214
Sun et al[25]	2019	NS	ENO1
Kong et al[26]	2019	Lymphoid node	MiR-25
Miwa et al[27]	2019	Hepatic and peritoneal	HOXC10

Abbreviation: NS, not specific; THBS4, thrombospondin 4; CEA, carcinoembryonic antigen; CA199, carbohydrate antigen-199; ENO1, alpha-enolase; HOXC10, homeobox C10.

Figures

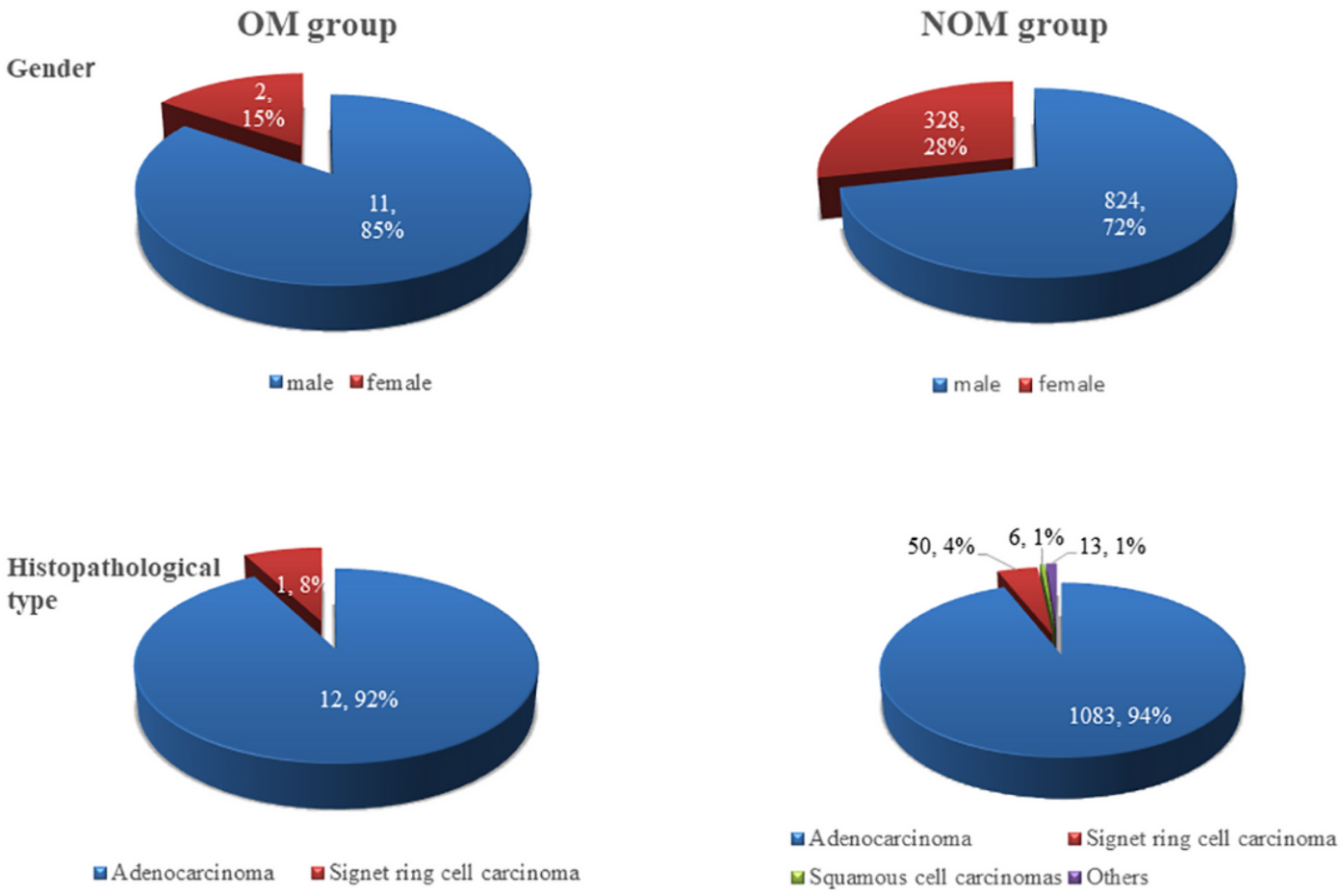

Figure 1

Clinical characteristics of gastric cancer OM patients and NOM patients. Notes: n=13 in OM group, n=1152 in NOM group. Abbreviation: OM, ocular metastasis; NOM, non-ocular metastasis.

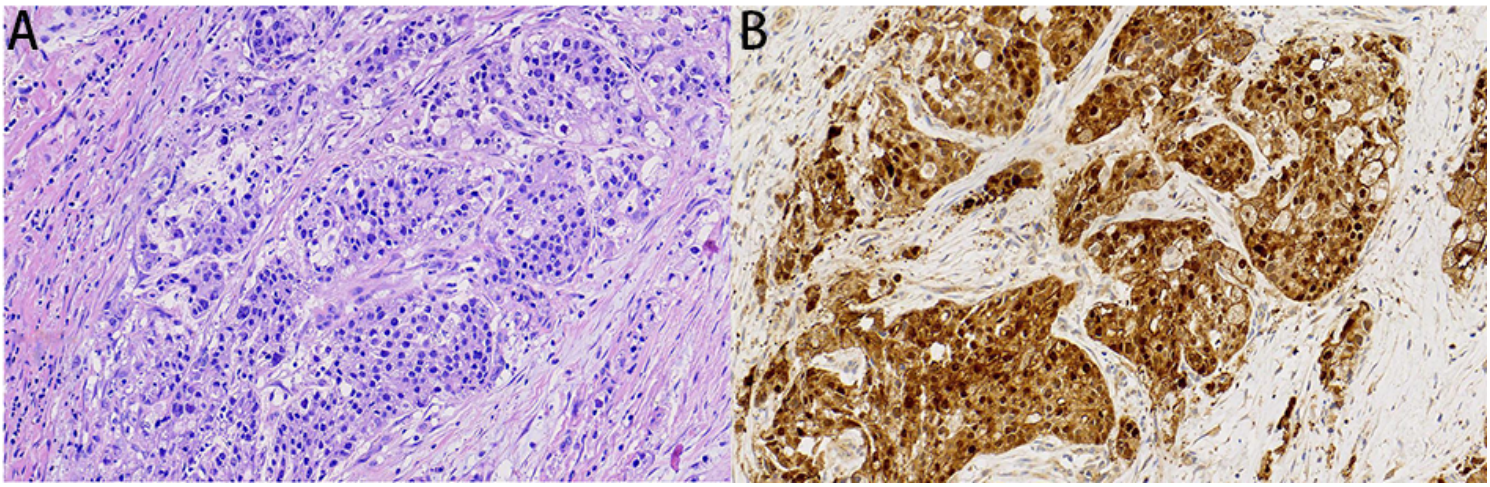

Figure 2

The HE staining and IHC images from gastric cancer OM patients. Notes: A. gastric cancer (HE×200). B. Villin (+) (SP×200). The tissue was collected from OM site of gastric cancer patients. Abbreviation: HE, hematoxylin-eosin; IHC, immunohistochemistry; OM, ocular metastasis; SP, streptavidin-peroxidase.

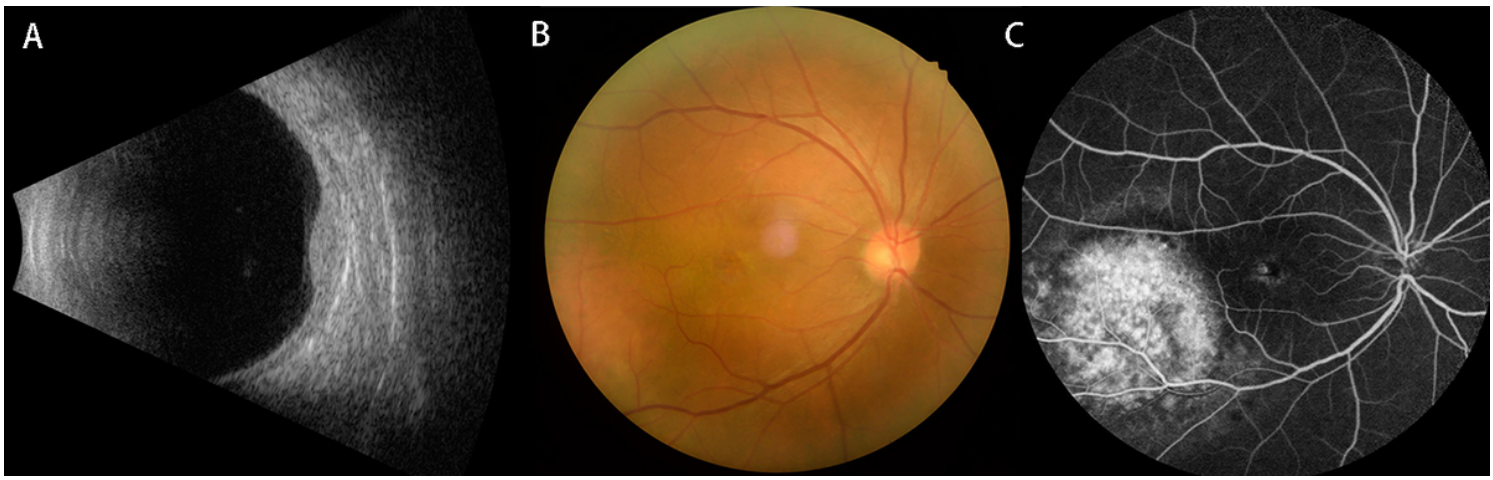

Figure 3

Imaging and pathological data of OM in GC patients. Notes: A. Ultrasound examination of ocular. The relative shape of the hypoechoic mass is seen. The posterior echo of the mass is diminished, and there is an infiltration around the mass. B. Fundus photography of an OM patient with GC. C. Fluorescence leakage and low fluorescence were observed in the lesions. Blood vessels are visible in the field of vision. Abbreviation: OM, ocular metastasis; GC, gastric cancer.

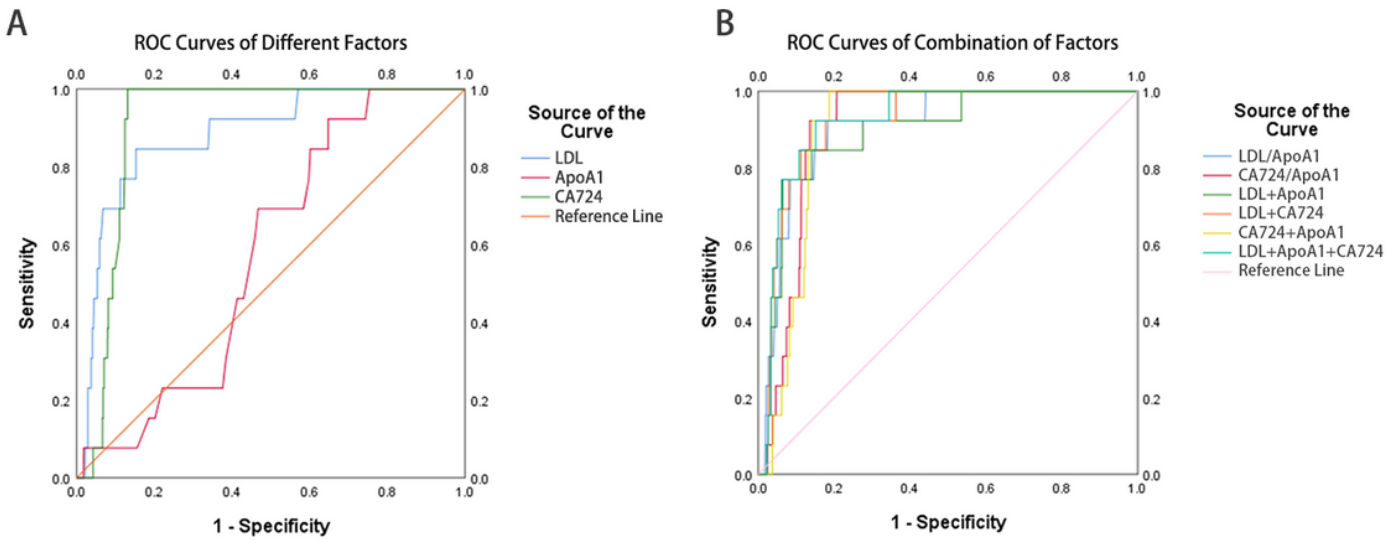

Figure 4

The receiver operating characteristics (ROC) curves of risk factors for detecting OM in elderly GC patients. Notes: (A). ROC curves of LDL, ApoA1 and CA724 as single risk factor of OM. (B). ROC curves of LDL to ApoA1 ratio, CA724 to ApoA1 ratio, LDL+ApoA1, LDL+CA724, CA724+ApoA1, LDL+ApoA1+CA724. Abbreviation: OM, ocular metastasis; GC, gastric cancer; LDL, low-density lipoprotein; ApoA1, apolipoprotein A1; CA724, carbohydrate antigen-724.