ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2023 July 15; 15(7): 1105-1316

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

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NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
July 15, 2023

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World J Gastrointest Oncol 2023 July 15; 15(7): 1253-1261

DOI: 10.4251/wjgo.v15.i7.1253

ISSN 1948-5204 (online)

ORIGINAL ARTICLE

Retrospective Study

Clinical association between coagulation indicators and bone metastasis in patients with gastric cancer

Xuan Wang, Jing-Ya Wang, Min Chen, Juan Ren, Xin Zhang

Specialty type: Oncology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Seretis C, Greece; Tanabe S, Japan

Received: February 6, 2023
Peer-review started: February 6, 2023
First decision: March 15, 2023
Revised: March 16, 2023
Accepted: May 6, 2023
Article in press: May 6, 2023
Published online: July 15, 2023

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Abstract

BACKGROUND

Bones are one of the most common target organs for cancer metastasis. Early evaluation of bone metastasis (BM) status is clinically significant. Cancer patients often experience a hypercoagulable state.

AIM

To evaluate the correlation between coagulation indicators and the burden of BM in gastric cancer (GC).

METHODS

We conducted a single-center retrospective study and enrolled 454 patients. Clinical information including routine blood examination and coagulation markers were collected before any treatment. Patients were grouped according to the status of BM. Receiver operating characteristic curves were used to assess diagnostic performance and determine the optimal cutoff values of the above indicators. Cutoff values, sensitivity and specificity were based on the maximum Youden index. Univariate and multivariate logistic regression analyses were used to evaluate the relationships between biomarkers and BM.

RESULTS

Of the 454 enrolled patients, 191 patients were diagnosed with BM. The receiver operating characteristic curve analysis suggested that prothrombin time (PT)

[cutoff: 13.25; sensitivity: 0.651; specificity: 0.709; area under receiver operating characteristic curve (AUC) = 0.738], activated partial thromboplastin time (aPTT) (cutoff: 35.15; sensitivity: 0.640; specificity: 0.640; AUC = 0.678) and fibrin degradation products (FDP) (cutoff: 2.75; sensitivity: 0.668; specificity: 0.801; AUC = 0.768) act as novel predictors for BM. Based on multivariate logistic regression analysis, the results showed the independent correlation between PT [odds ratio (OR): 3.16; 95% confidence interval (CI): 1.612-6.194; P = 0.001], aPTT (OR: 2.234; 95%CI: 1.157-4.313; P = 0.017) and FDP (OR: 3.17; 95%CI: 1.637-6.139; P = 0.001) and BM in patients with GC. Moreover, age, carcinoembryonic antigen, erythrocyte and globulin were found to be significantly associated with BM.

CONCLUSION

Coagulation markers, namely PT, aPTT and FDP, might be potential predictors for screening BM in patients with GC.

Key Words: Gastric cancer; Bone metastasis; Coagulation markers; Risk factor; Activated partial thromboplastin time; Prothrombin time; Fibrin degradation products

Core Tip: Bones are one of the most common organs involved in cancer metastasis. Early evaluation of bone metastasis (BM) status is clinically significant. In this study, we confirmed that coagulation markers (prothrombin time, activated partial thromboplastin time and fibrin degradation products), carcinoembryonic antigen and globulin are independent risk factors for BM in patients with gastric cancer. Patients with these risk factors should be screened early for BM, which may significantly decrease mortality rates related to BM in patients with gastric cancer.

Citation: Wang X, Wang JY, Chen M, Ren J, Zhang X. Clinical association between coagulation indicators and bone metastasis in patients with gastric cancer. *World J Gastrointest Oncol* 2023; 15(7): 1253-1261
URL: https://www.wjgnet.com/1948-5204/full/v15/i7/1253.htm
DOI: https://dx.doi.org/10.4251/wjgo.v15.i7.1253

INTRODUCTION

Gastric cancer (GC) is one of the most malignant neoplasms worldwide. According to GLOBOCAN's 2020 statistics, there were approximately 1.089 million new GC cases and 769000 GC deaths worldwide. GC has the fifth highest incidence rate and the fourth highest mortality rate of all cancers[1].

Common metastatic sites of GC are the liver, lungs, and peritoneum. Bone metastasis (BM) is relatively rare, ranging from 0.9% to 3.8%[2,3]. However, this incidence has been as high as 13.4% in autopsies[4]. The majority of patients with BM have several symptoms including bone pain, mobility disorders, hypercalcemia, pathological fractures and spinal cord compression, which seriously affects their quality of life. Unfortunately, BM is often underdiagnosed because sensitive diagnostic tests are recommended only after the onset of clinical symptoms. In addition, the median survival time for patients with GC-related BM is only 3-6 mo[3,5].

Imaging is currently the most important diagnostic method for BM. Elevated serum tumor markers such as carcinoembryonic antigen (CEA), carbohydrate antigen 19-9 (CA19-9) and bone-associated alkaline phosphatase (ALP) provide additional diagnostic significance[6,7]. Computed tomography (CT) or enhanced CT is not a routine test for BM screening. It is only recommended when the patient is symptomatic, which leads to asymptomatic BM in patients with GC being largely undetected[4]. Previous studies have found that fibrinogen, activated partial thromboplastin time (aPTT) and D-dimer are independent risk factors for BM in non-small cell lung cancer[8]. However, there has been little research on multiple risk factors, such as a combination of clinical data and laboratory indicators, for BM in patients with GC. This study explored risk factors for BM from GC through multivariate analysis based on laboratory tests.

MATERIALS AND METHODS

Patients

We retrospectively collected data on patients diagnosed with GC at the First Affiliated Hospital of Xi'an Jiaotong University from January 2014 to January 2019. The inclusion criteria were no distant metastases or BM. Exclusion criteria included: (1) A history of thrombotic disease, anticoagulant therapy or antiplatelet therapy; (2) Acute infection or disseminated intravascular coagulation; and (3) Lack of pretreatment laboratory data. In total, 454 patients were enrolled in this study. Data evaluated included sex, age at diagnosis, preoperative routine blood examination (erythrocyte, hemoglobin, leukocyte, neutrophil, lymphocyte, monocyte and platelet), glucose, albumin, globulin, CEA, CA19-9, CA72-4 and

coagulation markers including prothrombin time (PT), prothrombin ratio (PTR), international normalized ratio (INR), aPTT, thrombin time (TT), fibrinogen, D-dimer and fibrin degradation products (FDP). Laboratory indicators were collected before any treatment. Blood parameters were those closest to the time of treatment. This study was approved by the Ethics Committee of First Affiliated Hospital of Xi'an Jiaotong University.

Statistical analysis

Cases were grouped according to BM status. Categorical variables were expressed as frequency (percentage) and compared using the χ^2 test. Continuous variables were expressed as mean and standard deviation or median and interquartile range depending on whether they were normally distributed. Normally distributed continuous variables were compared using the Student's *t*-test. Continuous variables that were not normally distributed were compared using the Mann-Whitney *U* test. The parameters with significant differences between the control group and the BM group were selected for receiver operating characteristic (ROC) analysis. The optimal cutoff values for parameters were obtained by ROC analyses based on the Youden index. The prediction probability (PP) of combined ROC curve was obtained by binary logistic regression. Multivariate logistic regression was performed to assess the relationship between laboratory variables and BM status. Statistical analyses and data plotting were performed with SPSS Statistics (version 20.0; IBM Corp., Armonk, NY, United States). A two-sided *P* value < 0.05 was considered statistically significant.

RESULTS

Patient characteristics

We collected data from 454 patients with GC and grouped them according to the method described previously. As shown in Table 1, there were 191 cases in the BM group. The median age of patients was 61 years, and males comprised the majority of patients (73.8%). Patients with BM had higher levels of GC markers (CEA, CA19-9 and CA72-4), neutrophils, glucose, globulin and most coagulation parameters (PT, PTR, INR, aPTT, fibrinogen, D-dimer and FDP) (all $P < 0.001$). Moreover, erythrocyte, lymphocyte and platelet levels were significantly lower in the BM group (all $P < 0.05$) (Table 1).

BM in patients with GC can be predicted by novel tumor markers PT, aPTT and FDP

We performed ROC analysis to assess the efficacy of parameters to predict BM in patients with GC and obtained a series of cutoff values. The optimal cutoff values (sensitivity and specificity) were: age, 59.5 (54.6% and 58.3%); CEA, 3.97 (64.9% and 71.1%); CA19-9, 12.81 (65.5% and 64.9%); CA72-4, 6.71 (51.8% and 74.7%); erythrocyte level, 4.43 (42.3% and 79.7%); hemoglobin, 133.5 (42.7% and 75.9%); leukocyte level, 6.28 (49.2% and 68.5%); neutrophil level, 4.23 (48.4% and 74.9%); lymphocyte level, 1.43 (55.2% and 64.2%); platelet level, 167.5 (73.1% and 44.9%); glucose, 4.82 (52.4% and 74.8%); globulin, 28.75 (50.0% and 81.4%); PT, 13.25 (65.1% and 70.9%); PTR, 1.09 (40.7% and 78.5%); INR, 1.1 (37.6% and 81.9%); aPTT, 35.15 (64.0% and 64.0%); TT, 15.95 (69.7% and 48.7%); fibrinogen, 4.06 (42.3% and 82.0%); D-dimer, 1.03 (69.0% and 72.8%); FDP, 2.75 (66.8% and 80.1%) (Figure 1, Supplementary Figures 1 and 2). The area under ROC curves and 95% confidence intervals (CI) were: CEA, 0.694 (0.639-0.748); CA19-9, 0.673 (0.617-0.729); CA72-4, 0.624 (0.560-0.688); PT, 0.738 (0.692-0.784); aPTT, 0.678 (0.629-0.727); and FDP, 0.768 (0.722-0.814) (Table 2, Figure 1).

Parameters were grouped by aforementioned cutoff values. Multivariate logistic regression analysis showed that higher PT [odds ratio (OR): 3.16; 95%CI: 1.612-6.194; $P = 0.001$), higher aPTT (OR: 2.234; 95%CI: 1.157-4.313; $P = 0.017$) and elevated FDP (OR: 3.17; 95%CI: 1.637-6.139; $P = 0.001$) were independent risk factors for BM in patients with GC. In addition, higher CEA and globulin as well as lower age and red blood cell count were also independent risk factors for BM with an OR (95%CI) of 2.847 (1.496-5.418), 4.253 (2.114-8.558), 0.392 (0.203-0.756), and 0.482 (0.24-0.966), respectively (all $P < 0.05$) (Table 3). The area under ROC curve (95%CI) of PP was 0.879 (0.841-0.917) with a sensitivity of 0.831 and a specificity of 0.806 (Table 2, Figure 1).

DISCUSSION

BM is a common complication of certain cancers, including breast cancer and prostate cancer[9], whereas BM due to GC is less frequent[10]. The common metastatic sites of GC are the liver, lungs and peritoneum. Most patients with BM due to GC have multiple metastases, and most metastases are difficult to resect surgically[11]. Once tumors have metastasized to the bone, they are virtually incurable and cause severe morbidity before the patient dies. BM leads to pain, pathological fractures, nerve compression syndrome and hypercalcemia. According to relevant research reports, the proportion of patients suspected of BM due to GC found by bone scan screening was as high as 25.0%-45.3%[12].

Several factors have been shown to have predictive value for BM due to GC. BM is a dynamic process of osteolytic and osteogenesis mediated by osteoclasts that disrupts normal bone homeostasis. Bone ALP is an indicator of osteoblast metabolism and a relatively specific osteogenic marker, which has predictive value in patients with BM due to GC[6]. Bone screening is recommended for cancer types with a high incidence of BM, such as prostate cancer, breast cancer, small cell lung cancer and renal cell carcinoma. A variety of imaging studies are available, including plain X-rays, bone scintigraphy, CT scans, magnetic resonance imaging, positron emission tomography and positron emission tomography/CT, to assess bone involvement. However, bone screening has not been routinely recommended by the Chinese Society of Clinical Oncology for patients with GC[13]. Excessive X-rays and CT imaging are expensive and put patients at risk of unnecessary radiation exposure and/or invasive procedures due to false positive results. Therefore, it is necessary to

Table 1 Demographic and baseline characteristics of patients

Characteristic	Overall, *n* = 454	No bone metastasis, *n* = 263	Bone metastasis, *n* = 191	*P* value
Male sex	335 (73.8)	196 (74.5)	139 (72.8)	0.676
Age, yr	59 (50-67)	61 (51-67)	57 (49-66)	0.046
CEA, ng/mL	3.53 (1.73-14.65)	2.43 (1.35-4.89)	5.29 (2.90-38.31)	< 0.001
CA19-9, U/mL	12.25 (6.30-46.88)	9.89 (4.92-20.20)	22.62 (9.73-113.35)	< 0.001
CA72-4, U/mL	3.39 (1.60-12.00)	2.58 (1.57-6.78)	7.09 (1.96-21.68)	< 0.001
Erythrocyte, × 10^{12}/L	4.14 (3.65-4.57)	4.27 (3.78-4.68)	4.00 (3.50-4.39)	< 0.001
Hemoglobin, g/L	124 (106-139)	127 (109-143)	119 (103-133)	< 0.001
Leukocyte, × 10^{9}/L	5.69 (4.51-7.12)	5.51 (4.43-6.76)	6.20 (4.69-7.86)	0.002
Neutrophil, × 10^{9}/L	3.54 (2.64-4.88)	3.23 (2.51-4.33)	4.04 (2.83-5.97)	< 0.001
Lymphocyte, × 10^{9}/L	1.37 (1.08-1.81)	1.48 (1.12-1.95)	1.30 (1.02-1.63)	0.001
Platelet, × 10^{9}/L	196 (150-253)	204 (160-260)	180 (140-235)	0.001
Monocyte, × 10^{9}/L	0.41 (0.30-0.54)	0.42 (0.31-0.54)	0.40 (0.30-0.55)	0.713
Glucose, mmol/L	4.54 (4.17-5.07)	4.40 (4.04-4.83)	4.84 (4.39-5.55)	< 0.001
Albumin, g/L	38.11 ± 4.96	37.80 ± 4.71	38.55 ± 5.26	0.113
Globulin, g/L	26.4 (23.7-29.8)	25.5 (22.8-28.2)	28.8 (25.1-31.6)	< 0.001
PT, s	13.1 (12.5-13.8)	12.8 (12.3-13.4)	13.5 (13.0-14.4)	< 0.001
PTR	1.05 (0.99-1.10)	1.03 (0.98-1.08)	1.06 (1.01-1.12)	< 0.001
INR	1.05 (0.99-1.10)	1.03 (0.98-1.08)	1.07 (1.01-1.13)	< 0.001
aPTT, s	35.0 (31.5-38.1)	33.5 (30.8-36.8)	36.3 (33.7-39.1)	< 0.001
TT, s	16.3 (15.6-16.9)	16.4 (15.7-17.0)	16.0 (15.3-16.8)	< 0.001
FIB, g/L	3.32 (2.76-4.16)	3.21 (2.62-3.82)	3.63 (2.93-4.59)	< 0.001
D-dimer, mg/L	0.9 (0.3-2.5)	0.5 (0.1-1.1)	2.0 (0.8-6.6)	< 0.001
FDP, mg/L	1.9 (0.9-4.9)	1.2 (0.7-2.5)	4.5 (1.7-16.2)	< 0.001

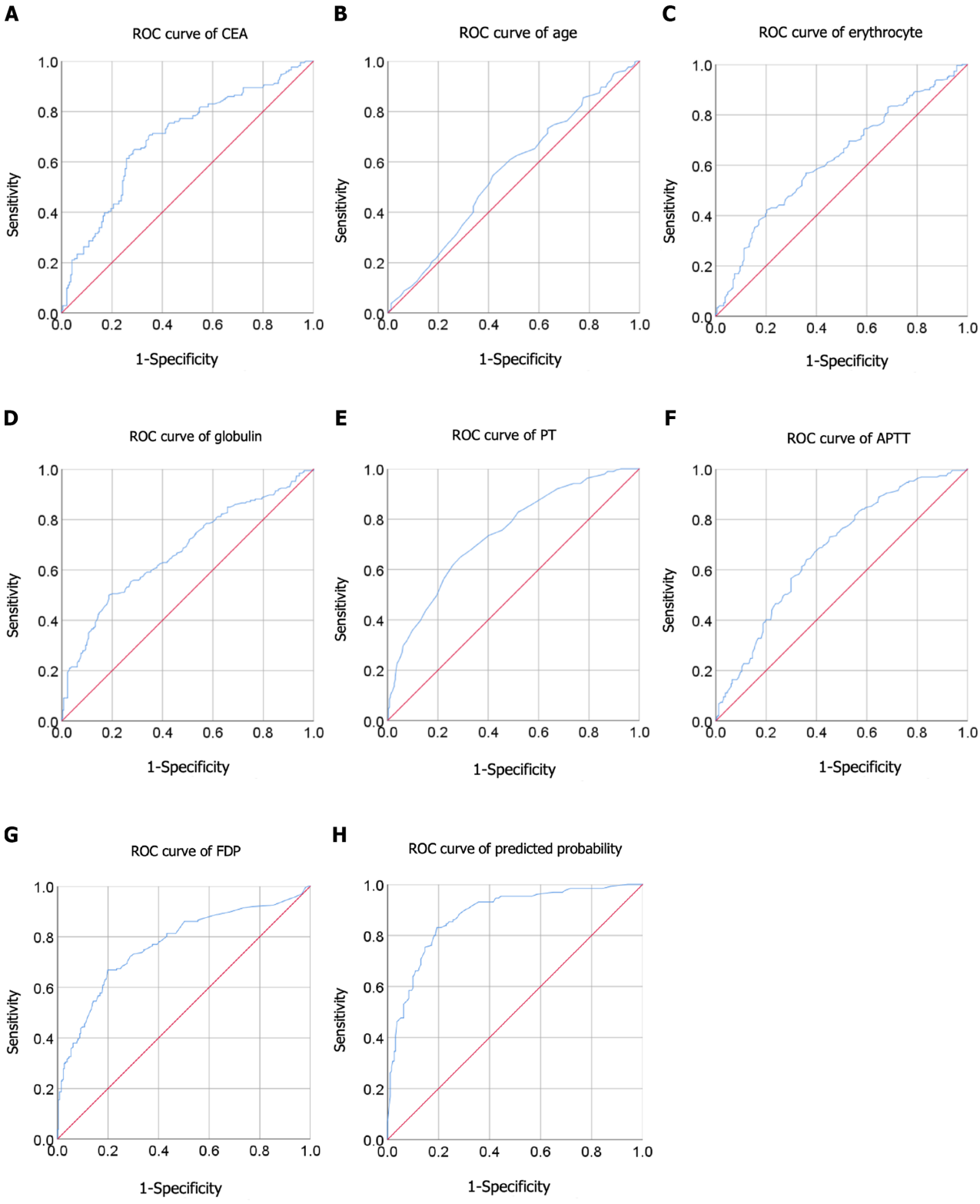
Data are shown as number of cases and percentage or median and interquartile range. aPTT: Activated partial prothrombin time; CA19-9: Carbohydrate antigen 19-9; CA72-4: Carbohydrate antigen 72-4; CEA: Carcinoembryonic antigen; FDP: Fibrin degradation products; FIB: Fibrinogen; INR: International normalized ratio; PT: Prothrombin time; PTR: Prothrombin ratio; TT: Thrombin time.

evaluate BM through a combination of imaging and analyzing hematological parameters and patient symptoms.

In this study, we screened possible risk factors for BM by comparing baseline data between the control group and the BM group. Through multivariate logistic regression analysis of candidate tumor markers, routine blood counts, coagulation indicators, albumin and globulin, we found that elevated CEA, globulin, PT, aPTT and FDP and younger age and lower red blood cells were independent risk factors for BM due to GC. CEA is a classic GC marker and has been shown to be a risk factor for distant metastasis and lymph node metastasis[14,15]. Globulin was identified as an independent predictor of occult metastasis in the neck of oral squamous cell carcinoma[16]. In GC, a high level of globulin is a valuable predictor of tumor progression[17].

Tumors are often accompanied by a state of coagulation activation[18]. Fibrinogen, aPTT and D-dimer were found to be risk factors for BM in non-small cell lung carcinoma patients[19]. Our study confirmed that PT, aPTT and FDP, as coagulation indicators, are independent predictors of BM in GC patients. In fact, tumor cells often express tissue factor or other procoagulants that can initiate coagulation[20]. There is considerable evidence that inhibiting coagulation can inhibit tumor metastasis[21,22]. BM due to GC can develop regardless of the tumor stage, although the proportion of patients with stage IV GC with BM exceeds the proportion of patients with stages I-III combined. It was found that even after radical gastrectomy, BM recurred in 1.8% of patients[23]. This indicates that the risk of BM should be considered when these indicators are abnormally elevated in patients with GC, especially when they are higher than the cutoff values in Table 2. Furthermore, the cutoff values of the BM risk factors indicated in this study are different from their respective upper limits of clinical normality. In other words, elevated coagulation indicators may indicate BM risk even within the range of clinically normal reference values.

A hypercoagulable state represents a heterogeneous group of disorders that cover a variety of risk factors such as thrombosis, obesity, pregnancy, cancer and its treatment, antiphospholipid antibody syndrome, heparin-induced thrombocytopenia and myeloproliferative disorders[24]. This suggests that in order to improve the specificity of



DOI: 10.4251/wjgo.v15.i7.1253

Figure 1 Receiver operating characteristic analysis for the prediction of bone metastasis. A-H: Area under the receiver operating characteristic (ROC) curve analysis indicated the diagnostic power of carcinoembryonic antigen (CEA) (A), age (B), erythrocyte level (C), globulin (D), prothrombin time (PT) (E), activated partial thromboplastin time (APTT) (F), fibrin degradation product (FDP) (G) and prediction probability (H) for bone metastasis. Prediction probability was obtained by binary logistic regression of CEA, age, erythrocyte level, globulin, PT, APTT and FDP. The area under the ROC curve of the prediction probability was 0.879 with a 95% confidence interval of 0.841-0.917. ROC: Receiver operating characteristic; FDP: Fibrin degradation product; PT: Prothrombin time; APTT: Activated partial thromboplastin time; CEA: Carcinoembryonic antigen.

coagulation factors in assessing BM due to GC, other factors that may affect their levels need to be excluded. Although we discovered independent risk factors for BM due to GC, we did not explore whether they were specific to BM or due to other metastatic sites' GC.

Table 2 Area under the receiver operating characteristic curves and cutoff values of diagnostic indicators at the maximum Youden index for bone metastasis

Parameter	AUC	95%CI	Cutoff	Sen	Spe	Youden index	PPV	NPV	*P* value
Age	0.558	0.501-0.616	59.5	0.546	0.583	0.129	0.433	0.546	0.046
CEA	0.694	0.639-0.748	3.97	0.649	0.711	0.36	0.665	0.711	< 0.001
CA19-9	0.673	0.617-0.729	12.81	0.655	0.649	0.304	0.614	0.649	< 0.001
CA72-4	0.624	0.560-0.688	6.71	0.518	0.747	0.265	0.603	0.747	< 0.001
Erythrocyte	0.623	0.571-0.675	4.43	0.423	0.797	0.220	0.498	0.423	< 0.001
Hemoglobin	0.599	0.547-0.651	133.50	0.427	0.759	0.186	0.488	0.427	< 0.001
Leukocyte	0.587	0.532-0.641	6.28	0.492	0.685	0.177	0.529	0.685	0.002
Neutrophil	0.63	0.576-0.683	4.23	0.484	0.749	0.233	0.581	0.749	< 0.001
Lymphocyte	0.591	0.539-0.644	1.43	0.552	0.642	0.194	0.508	0.552	0.001
Platelet	0.591	0.538-0.645	167.50	0.731	0.449	0.180	0.545	0.731	0.001
Glucose	0.664	0.613-0.716	4.82	0.524	0.748	0.272	0.595	0.748	< 0.001
Globulin	0.675	0.624-0.726	28.75	0.500	0.814	0.314	0.655	0.814	< 0.001
PT	0.738	0.692-0.784	13.25	0.651	0.709	0.360	0.618	0.709	< 0.001
PTR	0.622	0.570-0.675	1.09	0.407	0.785	0.193	0.579	0.785	< 0.001
INR	0.627	0.574-0.680	1.10	0.376	0.819	0.195	0.602	0.819	< 0.001
aPTT	0.678	0.629-0.727	35.15	0.640	0.640	0.280	0.563	0.640	< 0.001
TT	0.598	0.545-0.652	15.95	0.697	0.487	0.184	0.538	0.816	< 0.001
FIB	0.616	0.562-0.669	4.06	0.423	0.820	0.243	0.630	0.820	< 0.001
D-dimer	0.756	0.710-0.801	1.03	0.690	0.728	0.418	0.645	0.728	< 0.001
FDP	0.768	0.722-0.814	2.75	0.668	0.801	0.469	0.706	0.801	< 0.001
PP	0.879	0.841-0.917	0.364	0.831	0.806	0.637	0.745	0.806	< 0.001

aPTT: Activated partial prothrombin time; AUC: Area under receiver operating characteristic curve; CA19-9: Carbohydrate antigen 19-9; CA72-4: Carbohydrate antigen 72-4; CEA: Carcinoembryonic antigen; CI: Confidence interval; FDP: Fibrin degradation products; FIB: Fibrinogen; INR: International normalized ratio; NPV: Negative predictive value; PP: Prediction probability; PPV: Positive predictive value; PT: Prothrombin time; PTR: Prothrombin ratio; Sen: Sensitivity; Spe: Specificity; TT: Thrombin time.

Because we retrospectively collected data from patients with GC, bone-associated ALP was not routinely tested and was not included in the analysis. There is evidence that tumor-induced hypercoagulability and fibrin formation are required for tumor angiogenesis, metastasis and invasion because cross-linked fibrin in the extracellular matrix may be the framework for tumor cell migration during invasion. Based on this, circulating tumor cells and micrometastases are considered early events in the process of tumor cell metastasis[25]. Bone ALP is a specific marker of osteoblast metabolism and is significantly associated with the presence and degree of bone involvement in metastatic tumors. Bone-associated ALP has been shown to be an important predictor of BM in patients with breast and prostate cancer[26]. More than half of patients with BM due to GC have elevated ALP and tumor markers[3,6]. Coagulation indexes and bone ALP reflect the two stages of tumor hematogenous metastasis and BM, respectively. In this study, we demonstrated that the PP obtained by combination ROC had a higher diagnostic efficacy than any single risk factor. The combination of coagulation indexes, globulins, tumor markers and bone ALP may greatly improve the diagnostic efficiency of BM due to GC.

CONCLUSION

Overall, coagulation markers (PT, aPTT and FDP), CEA and globulin are independent risk factors for BM due to GC. Patients with these risk factors should be screened for BM early, which could lead to significantly decreased mortality in patients with GC and BM.

Table 3 Univariate and multivariate binary logistic regression analyses of variables for bone metastasis

	Univariate analysis			Multivariate analysis		
Parameter	Odds ratio	95%CI	*P* value	Odds ratio	95%CI	*P* value
Age	0.594	0.398-0.887	0.011	0.392	0.203-0.756	0.005
CEA	4.559	2.931-7.090	< 0.001	2.847	1.496-5.418	0.001
CA19-9	3.511	2.271-5.429	< 0.001			0.352
CA72-4	3.176	1.995-5.056	< 0.001			0.086
Erythrocyte	0.348	0.226-0.536	< 0.001	0.482	0.240-0.966	0.040
Hemoglobin	0.425	0.281-0.645	< 0.001			0.852
Leukocyte	2.102	1.426-3.099	< 0.001			0.693
Neutrophil	2.798	1.872-4.183	< 0.001			0.601
Lymphocyte	0.453	0.308-0.667	< 0.001			0.575
Platelet	0.452	0.304-0.672	< 0.001			0.066
Glucose	3.273	2.191-4.890	< 0.001			0.087
Globulin	4.367	2.861-6.667	< 0.001	4.253	2.114-8.558	< 0.001
PT	4.536	3.038-6.774	< 0.001	3.16	1.612-6.194	0.001
PTR	2.517	1.663-3.808	< 0.001			0.145
INR	2.727	1.771-4.199	< 0.001			0.072
aPTT	3.161	2.140-4.669	< 0.001	2.234	1.157-4.313	0.017
TT	0.535	0.344-0.833	0.006			0.842
FIB	3.342	2.179-5.125	< 0.001			0.193
D-dimer	5.952	3.939-8.993	< 0.001			0.956
FDP	8.103	5.271-12.457	< 0.001	3.17	1.637-6.139	0.001

The reference of parameters was set to be less than their cutoff values. aPTT: Activated partial prothrombin time; CA19-9: Carbohydrate antigen 19-9; CA72-4: Carbohydrate antigen 72-4; CEA: Carcinoembryonic antigen; CI: Confidence interval; FDP: Fibrin degradation products; FIB: Fibrinogen; INR: International normalized ratio; PT: Prothrombin time; PTR: Prothrombin ratio; TT: Thrombin time.

ARTICLE HIGHLIGHTS

Research background

Bones are one of the most common targets for cancer metastasis. However, bone metastasis (BM) is often underdiagnosed because sensitive diagnostic imaging methods are recommended only after the onset of clinical symptoms. Patients with gastric cancer (GC), especially in advanced stages, are often in a hypercoagulable state.

Research motivation

The purpose of this study was to explore the predictive value of blood indicators on the risk of BM due to GC and to improve the diagnostic efficacy of BM due to GC by screening effective risk factors.

Research objectives

The purpose of this study was to explore whether coagulation indicators can be used as independent risk factors for predicting BM due to GC, thus promoting the early diagnosis and treatment of BM.

Research methods

We conducted a retrospective study and enrolled 454 patients in this study. Receiver operating characteristic (ROC) curves were used to assess diagnostic performance. Univariate and multivariate logistic regression analyses were used to evaluate the relationship between biomarkers and BM.

Research results

ROC curve analysis indicated that coagulation markers have similar or better diagnostic efficacy than traditional GC markers. Based on multivariate logistic regression analysis, prothrombin time, activated partial thromboplastin time and fibrin degradation products were independently associated with BM due to GC. Moreover, age, carcinoembryonic

antigen, erythrocyte level and globulin were found to be risk factors of BM. Combining these indicators could improve the effectiveness of diagnosing BM.

Research conclusions

Coagulation markers (prothrombin time, activated partial thromboplastin time and fibrin degradation products), carcinoembryonic antigen and globulin were independent risk factors for BM due to GC. Patients with these risk factors should be screened early to detect BM due to GC and prevent bone-related events.

Research perspectives

Future research will explore the relationship and molecular mechanism between coagulation and tumor metastasis and explore new targets to block the process of tumor metastasis.

FOOTNOTES

Author contributions: Wang X, Ren J and Zhang X designed the research study; Wang X, Wang JY and Chen M performed the research; Wang X analyzed the data and wrote the manuscript; all authors read and approve the final manuscript.

Institutional review board statement: This study was approved by the Ethics Committee of First Affiliated Hospital of Xi'an Jiaotong University (Approval No. 2015-046).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: The authors declare that no competing interests exist.

Data sharing statement: Dataset available from the corresponding author at zhangxinzh@stu.xjtu.edu.cn

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S-Editor: Yan JP
L-Editor: A
P-Editor: Zhang XD

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