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Retrospective Cohort Study

Analysis of vascular thrombus and clinicopathological factors in prognosis of gastric cancer: A retrospective study

Correlation analysis of vascular thrombus in GC

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Abstract

BACKGROUND

Gastric cancer is one of the most common malignant tumors in the world, and its prognosis is closely related to many factors. In recent years, the incidence of vascular thrombosis in patients with gastric cancer has gradually attracted attention, and studies have found that it may have a significant impact on the survival rate and prognosis of patients. However, the specific mechanism of association between vascular thrombosis and prognosis of patients with gastric cancer remains unclear.

AIM

To analyze the relationships between vascular cancer suppositories and other clinicopathological factors and their influence on the prognosis of patients with gastric cancer.

METHODS

This study retrospectively analyzed the clinicopathological data of 621 patients with gastric cancer and divided them into a positive group and a negative group according to the presence or absence of a vascular thrombus. The difference in the 5-year cumulative survival rate between the two groups was compared, and the relationships between vascular cancer thrombus and other clinicopathological factors and their influence on the prognosis of patients with gastric cancer were analyzed.

RESULTS

Among 621 patients with gastric cancer, the incidence of vascular thrombi was 31.7% (197 patients). Binary logistic regression analysis revealed that the degree of tumor differentiation, depth of invasion, and extent of lymph node metastasis were independent influencing factors for the occurrence of vascular thrombi in gastric cancer patients ($P < 0.01$). The trend $\chi 2$ test showed that the degree of differentiation, depth of invasion, and extent of lymph node metastasis were linearly correlated with

the percentage of vascular thrombi in gastric cancer patients ($P < 0.01$), and the correlation between lymph node metastasis and vascular thrombi was more significant ($r = 0.387$). Univariate analysis revealed that the 5-year cumulative survival rate of the positive group was significantly lower than that of the negative group (46.7% vs. 73.3%, $P < 0.01$). Multivariate analysis revealed that age, tumor diameter, TNM stage, and vascular thrombus were independent risk factors for the prognosis of gastric cancer patients (all $P < 0.05$). Further stratified analysis revealed that the 5-year cumulative survival rate of stage III gastric cancer patients in the thrombolase-positive group was significantly lower than that in the thrombolase-negative group (36.1% vs. 51.4%; $P < 0.05$).

CONCLUSION

Vascular cancer suppository is an independent risk factor affecting the prognosis of patients with gastric cancer. The combination of vascular cancer suppositories and TNM staging can better judge the prognosis of patients with gastric cancer and guide more reasonable treatment.

Key Words: Vascular cancer thrombus; Gastric cancer; Survival prognosis; TNM staging; Retrospective study

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Core Tip: The relationship between vascular thrombosis and survival rate, recurrence rate and other prognostic indexes was investigated by statistical analysis. To summarize the potential influence mechanism of vascular thrombosis on the prognosis of patients with gastric cancer, and provide data support and theoretical basis for clinical treatment decision-making and individualized treatment strategy.

INTRODUCTION

Gastric cancer, one of the main causes of cancer death in our country, is a cause of concern[1-3]. However, the lack of popularity of routine gastroscopy has become a prominent problem. According to statistics, 80% of patients have advanced gastric cancer, which means that the tumor has spread throughout the body and is quite serious[4-6]. Even after radical surgery and postoperative adjuvant therapy, the 5-year survival rate of patients with advanced gastric cancer is still only approximately 30%, which is undoubtedly a rather worrisome figure[7]. The unsatisfactory prognosis of patients with gastric cancer is closely related to the high recurrence and metastasis rates of gastric cancer. In this process, the vasculature plays a key role[8]. The vasculature is an important way for tumor cells to spread far away, and the vasculature suppository is the manifestation of tumor invasion of lymphatic vessels or blood vessels. However, there are still many different views on the effect of vascular cancer thrombus on the prognosis of gastric cancer patients. The presence of a vascular cancer thrombus is considered to be one of the indicators of the degree of malignancy of gastric cancer[9]. The spread of tumor cells through the vasculature often leads to rapid growth and spread of the tumor, which exacerbates the worsening of the disease. Some studies have shown that patients with vascular cancer thrombus are more likely to experience postoperative recurrence and metastasis and have lower survival rates[10]. This view has been supported by some medical circles, which believe that vascular cancer embolus is not only a pathological feature but also a manifestation of the degree of malignancy of gastric cancer, thus affecting the prognosis of patients. However, some scholars have questioned this view. They believe that a vascular cancer thrombus does not necessarily indicate a poor prognosis. In some cases, even in the presence of a vascular cancer thrombus, after standard treatment, one can still obtain a good survival rate. This view highlights the importance of individual differences and treatment options in the prognosis of gastric cancer[11]. Compared with a single pathological indicator, it is more important to consider the overall condition of the patient, treatment

plan, and postoperative recovery[12]. On the other hand, some studies have also found that the formation of a vascular cancer thrombus may be closely related to the molecular biological characteristics of tumors. By altering gene expression and protein synthesis, tumor cells promote the formation of cancer plugs in blood vessels or lymphatic vessels in the vascular system[13]. This discovery provides a new idea for personalized therapy, and through an in-depth understanding of the molecular-level characteristics of patients' tumors, more precise treatment plans and improved treatment effectiveness are expected[14].There is no consensus on the effect of vascular cancer suppositories on the prognosis of gastric cancer patients. Most of the current research focuses on pathology and molecular biology, but more clinical practice and large-scale studies are needed to verify these findings. In addition, for gastric cancer patients as a whole, it is critical to increase the prevalence of routine gastroscopy to detect and treat gastric cancer earlier and improve patient survival[15].

In this study, the clinicopathological data of 621 patients with gastric cancer were retrospectively analyzed to explore the relationships between vascular cancer thrombus and other clinicopathological factors and their influence on the prognosis of postoperative patients with gastric cancer.

MATERIALS AND METHODS

General clinical data analysis of patientsA total of 621 patients with gastric cancer who underwent radical gastrectomy at our hospital between January 2020 and January 2024, including 448 males and 173 females, were included in this study. The mean age was 68 years, and the range was 34~81 years.

Inclusion and exclusion criteria The inclusion criteria for patients were as follows: Primary gastric cancer treated with radical gastrectomy (R0 resection, D2 Lymph node dissection) and postoperative pathological examination confirming gastric adenocarcinoma. No neoadjuvant chemoradiotherapy was performed before surgery. The clinicopathological data were complete and reliable. All patients provided written informed consent for surgery.The exclusion criteria were as follows: Had

distant metastasis, had a serious underlying disease, had other systemic malignancies, or died of complications during the perioperative period.

Pathological evaluationHE staining was performed on pathological sections of gastric cancer tissue supplemented with D2–40 and CD34 immunohistochemical staining. The pathological examination was performed independently by two expert pathologists, and disagreements were resolved by discussion with a third expert. Photoscopically, cancer cells entering the tumor or outside the tumor's blood vessels or lymphatic vessel endothelium were diagnosed as vascular cancer embolus-positive (Figure 1). According to the 15th edition of the Japanese Gastric Cancer Treatment Protocol, tubular adenocarcinoma, papillary adenocarcinoma, and highly or moderately differentiated adenocarcinoma are considered to be well differentiated, while poorly differentiated adenocarcinoma, sigma-ring cell carcinoma, and mucinous adenocarcinoma are considered to be poorly differentiated.

Research methods The following data were collected: General data, including age and sex; clinicopathologic data, including tumor differentiation degree, tumor diameter, Borrmann classification, depth of invasion, lymph node metastasis, TNM stage, number of lymph nodes detected, and vascular cancer embolus. Follow-up was conducted by telephone, email, and outpatient review until January 2024, and the 5-year cumulative survival rate was calculated.

Statistical analysisIBM SPSS 25.0 statistical software was used for statistical analysis. The $\chi 2$ test or Fisher's exact probability test was used for single-factor analysis of the statistical data. Binary logistic regression analysis was used for multivariate analysis. Correlations between variables were analyzed using the trend-$\chi 2$ test. The Kaplan–Meier method was used to construct survival curves, and the log-rank method was used for single-factor analysis. The observation indicators with statistical significance ($P < 0.1$) in the single factor analysis were included in the Cox proportional risk regression model for multifactor analysis. $P < 0.05$ indicated that the difference was statistically significant.

RESULTS

Relationship between vascular thrombus and other clinicopathological factors in gastric cancerA total of 621 patients with gastric cancer were included in this study, including 197 patients (31.7%) in the thrombus-positive group and 424 patients (68.3%) in the thrombus-negative group. Univariate analysis revealed that the degree of tumor differentiation, tumor diameter, Borrmann classification, depth of invasion, lymph node metastasis, and TNM stage were the influencing factors for the occurrence of vascular embolus in patients with gastric cancer ($P < 0.01$) (Table 1).

Binary logistic regression analysis The degree of tumor differentiation, depth of invasion, and degree of lymph node metastasis were found to be independent factors influencing the occurrence of vascular thrombus in gastric cancer patients (Table 2). The trend $\chi 2$ test showed that the degree of tumor differentiation, depth of invasion, and extent of lymph node metastasis were linearly correlated with the percentage of vascular thrombolus positivity in patients with gastric cancer (all $P < 0.01$), and the correlation between lymph node metastasis and vascular thrombolus invasion was more significant ($r = 0.387$) (Table 3).

Analysis of prognostic factors in patients with gastric cancer

For gastric cancer patients, the prognostic factors were the degree of tumor differentiation, tumor diameter, Borrmann classification, depth of invasion, lymph node metastasis, TNM stage of the tumor, and presence of a vascular cancer embolus (all $P < 0.05$). The 5-year cumulative survival rate of patients with thrompos-positive gastric cancer was significantly lower than that of patients with thrompos-negative gastric cancer (46.7% vs. 73.3%, $P < 0.01$) (Figure 2).

Clinical multifactor analysis The results showed that age, tumor diameter, TNM stage, and vascular cancer thrombus were independent risk factors affecting the prognosis of gastric cancer patients (Table 4). Further stratified analysis revealed that the 5-year cumulative survival rate of patients with TNM stage III gastric cancer in the

thrombolase-positive group was significantly lower than that in the thrombolase-negative group (36.1% vs. 51.4%, $P < 0.05$).

DISCUSSION

Vascular cancer suppositories are the invasion of blood vessels and lymphatic vessels by tumor cells, which is a common pathological manifestation and occurs in postoperative specimens of various malignant tumors[16-18]. As a potential prognostic factor, vascular cancer suppositories are receiving increasing attention from clinicians. In hepatocellular carcinoma, vascular cancer suppositories have become reliable indicators of hepatocellular carcinoma stage and prognosis prediction because they can accurately predict patient prognosis[19]. Some studies[20-22] have shown that vascular cancer suppositories are associated with poor prognosis in patients with gastric cancer, but vascular cancer suppositories have not been included in the TNM staging of gastric cancer. This retrospective study attempted to investigate the effect of a vascular cancer thrombus on the prognosis of patients with gastric cancer.

Previous studies[23-25] have shown that the incidence of vascular thrombus in gastric cancer patients ranges from 12.9% to 44.3%, while the incidence of vascular thrombus in this study was 37.1%. The incidence of vascular cancer thrombus varies among different study centers, which may be affected by the sample size and detection methods included in the study. The main detection methods for vascular cancer suppositories include HE staining and immunohistochemistry (IHC)[26]. At present, the recognized method for the detection of vascular cancer suppositories in the literature is IHC[27]. Artifacts generated by peritumoral tissue edema or tumor tissue shrinkage may affect the detection of vascular cancer suppositories in HE staining, which is more objective and accurate than HE staining[28]. In this study, HE staining supplemented with CD34 and D2-40 dual immunohistochemistry was used to improve the accuracy of the diagnosis of vascular cancer thrombus.

In this study, the degree of tumor differentiation, depth of invasion, and extent of lymph node metastasis were found to be independent influencing factors for the

occurrence of vascular thrombus in patients with gastric cancer. The trend $\chi 2$ test showed that the deeper the tumor invasion depth and the greater the number of lymph node metastases, the greater the incidence of vascular cancer thrombus. The results of relevant studies[29-31] were similar to those of the present study. Another study[32] revealed increased levels of VEGF in the tumor tissues of patients with positive vascular cancer embolus, which provided a reasonable explanation for the correlation between vascular cancer embolus and the depth of tumor invasion and lymph node metastasis. With increasing tumor growth and depth of tumor invasion, more blood vessels are needed, and tumor tissues promote neovascularization through the production of VEGF[33-35]. However, due to the incomplete basement membrane, new blood vessels increase the chances of tumor cells invading the vascular system, and the number of vascular cancer thrombi and lymph node metastases also increases[36].

There is no consensus on the effect of vascular cancer suppositories on the prognosis of patients with gastric cancer[37]. The results of relevant studies[38-40] show that the prognosis of patients with positive vascular thrombi is worse than that of patients with negative vascular thrombi, but vascular thrombi are not an independent prognostic factor for gastric cancer. Another study[41] of 1007 patients with gastric cancer showed that vascular cancer suppositories can reduce the 5-year cumulative survival rate of patients with gastric cancer and are an independent prognostic factor for gastric cancer. The results of a study[42] on 1398 patients with gastric cancer showed that vascular cancer suppositories were an independent prognostic factor for gastric cancer, and stratified analysis showed that vascular cancer suppositories only affected the prognosis of patients with TNM stage III gastric cancer, which was consistent with the results of this study. We believe that we should pay more attention to the role of thrombi in the prognosis of patients with gastric cancer, especially stage III gastric cancer[43]. Although there is no distant metastasis, the prognosis of thrombus-positive patients is still worse than that of thrombus-negative patients[44]. It is suggested that more active follow-up should be carried out for stage III gastric cancer patients with

positive vascular thrombi to detect tumor recurrence and distant metastasis in a timely manner and formulate more reasonable treatment strategies[45].

In conclusion, vascular cancer suppositories are an independent prognostic factor for patients with gastric cancer. The combination of vascular cancer suppositories and the 8th edition of the TNM staging system for gastric cancer can help patients with gastric cancer better judge their prognosis and guide more reasonable treatment. Especially for patients with stage III gastric cancer with a positive vascular embolus, in addition to postoperative adjuvant treatment, more active follow-up observation is recommended.

CONCLUSION

The correlation between vascular thrombosis and its clinicopathological features and prognosis of patients with gastric cancer was discussed retrospectively. Multivariate analysis further confirmed that vascular thrombosis and some clinicopathological factors such as tumor stage and patient age were independent risk factors affecting the prognosis of gastric cancer patients. These findings suggest that in the clinical management of gastric cancer, attention should be paid to the early screening and intervention of vascular thrombosis to optimize the treatment strategy of patients and improve the prognosis and survival rate.

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