

A Study on the Specific, Organ-specific Patterns of Recurrence after Surgical Treatment for Gastric Adenocarcinoma, Based on the SEER Database

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Abstract: Metastasis remains the main reason why gastric cancer treatment fails and why patients die. Yet metastatic lesions are not interchangeable. Peritoneal, hepatic, pulmonary, bone, and brain metastases differ in how often they appear, which patients they affect, and how long patients survive after diagnosis. The Surveillance, Epidemiology, and End Results (SEER) database is a large North American cancer registry. It has been used widely in retrospective work on organ-specific metastasis in gastric cancer. In this review, we examine SEER-based studies on metastasis to the peritoneum, liver, lung, bone, and brain. We compare reported incidence, clinicopathological correlates, survival estimates, and the value of prediction models. We also discuss differences among patient subgroups and the limitations that come with using SEER for this purpose. The aim is to help clinicians think about risk stratification, staging, and individualized decisions for patients with metastatic gastric cancer.

Keywords: Gastric cancer; SEER database; Distant metastasis; Organ-specific; Prognosis; Survival curve

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1. Introduction

Gastric cancer is a common digestive malignancy. Some patients still develop distant metastasis after curative surgery, and metastasis is a leading cause of death. Spread is not random. The liver, peritoneum, lungs and bones are involved most often. Survival varies by site. The 8th edition AJCC TNM system groups all distant

metastases as stage IV. This grouping is clinically convenient but does not capture the marked prognostic differences within stage IV.

Single-center studies are often too small to examine organ-specific metastasis reliably. SEER covers a large US population and includes demographics, pathology, treatment and follow-up. It has therefore been used for studies of metastatic patterns, risk factors and prediction models. Several SEER reports have described site-specific differences, but a systematic summary is still lacking. The present review includes cohort studies, propensity score matching, competing risk models, machine learning and forest plot analyses. Some included studies address lymph node metastasis and pathological staging, which provide context for distant spread. We summarize postoperative metastasis patterns by organ.

2. Distinct features of organ-specific metastasis, risk factors, and prognosis in gastric cancer

2.1. Liver metastasis

Hepatic involvement is common in gastric cancer. It can be found at diagnosis or later after surgery. Risk is not uniform. Age, histological type and primary tumor location all matter. In SEER analyses, liver lesions account for the largest part of hematogenous spread. T stage, N stage and differentiation grade are closely related to liver metastasis. After propensity score matching, younger patients show a higher risk than older patients. They are also more likely to develop metastases in several organs. Signet ring cell carcinoma can spread to the liver. Huang et al. ^[1] used SEER to construct survival curves for signet ring cell carcinoma with liver metastasis. These patients had a clearly worse prognosis than those without liver involvement.

An et al. ^[2] used a SEER external validation cohort. Age, T stage, N stage, differentiation and tumor size were independent risk factors for liver metastasis. Later T stage and greater lymph node involvement were associated with a higher risk. Machine learning studies have used SEER to predict liver metastasis. They usually include demographic data, T and N stage, differentiation and tumor origin. T2 and T4 tumors have a higher risk. Even T1 tumors can metastasize to the liver. Invasion depth and lymph node status are important predictors. Li et al. ^[3] built a decision tree model for liver metastasis and again identified lymph node involvement as a key predisposing factor.

Prognosis is poor after liver metastasis. Multi-organ involvement makes survival even shorter. Age, tumor grade and N stage are independent prognostic factors. Several SEER studies have used survival curves for risk stratification. Wu et al. ^[4] found in a SEER cohort analysis of causes of death that the primary cause of death in liver metastasis of gastric cancer is the tumor itself. Advanced age and high T and N stages significantly increase the risk of overall and tumor-specific death. The survival benefit from surgical removal of the primary tumor is highly heterogeneous, and SEER propensity score matching studies have shown that only highly selected patient subgroups benefit from surgical removal. Therefore, palliative gastric resection surgery is not recommended for all patients with liver metastasis of gastric cancer. Su et al. ^[5] developed a nomogram for prognosis after primary tumor resection in patients with liver metastasis. Tumor burden, lymph node status and treatment regimen were key variables. Wang et al. ^[6] developed a machine learning dynamic model to assess prognosis and guide treatment in liver metastasis. Ji et al. ^[7] pointed out that the advantages of surgery for gastric cancer patients with liver metastasis are not universally applicable; rather, individualized patient selection through predictive models is necessary.

2.2. Bone metastasis

Bone metastasis is less common than liver metastasis in gastric cancer. Isolated bone involvement is rare. Most patients with bone metastasis also have disease in other organs. These patients are often older and have advanced T and N stage and poorly differentiated adenocarcinoma. A high lymph node burden is common. Median survival is usually short. In early-stage gastric cancer, bone metastasis predicts a poor outcome. Possible mechanisms include immune suppression, abnormal coagulation and inflammatory pathway activation. When bone metastasis occurs in younger patients, prognosis seems to worsen more than in older patients. Ren et al. ^[8] reported that patients with bone metastasis often have a high lymph node metastatic burden, and survival after metastasis is much shorter.

Liu et al. ^[9] used SEER to build two web-based dynamic models. Age, T stage, N stage, tumor grade and tumor location were included. The models gave individualized estimates of bone metastasis risk and survival and showed acceptable internal validation. Lin et al. ^[10] conducted a comparative analysis of survival in patients with multi-organ metastasis using the SEER database. Patients with bone metastasis had a poorer prognosis compared to those with isolated liver metastasis, but a better prognosis than those with extensive multi-organ metastasis. When ≥ 2 organs were involved, the risk of death for bone metastasis patients was significantly elevated, indicating that multi-organ metastasis is a strong predictor of death in patients with gastric cancer.

2.3. Lung metastases

Isolated lung metastases in gastric cancer are relatively rare. SEER data show that most patients with lung metastases also have metastases in other organs, such as the liver and bones. Multiple regression analysis indicates that tumor stage, tumor node ratio (T), and tumor size are independent risk factors for lung metastasis. Lung metastasis accounts for a smaller proportion of all distant metastases in gastric cancer compared to liver metastasis. Zheng et al. ^[11] developed a web-based tool using SEER data to visualize the prognosis of gastric cancer patients with lung metastasis. Their findings confirmed that age, tumor grading, and N stage are independent prognostic factors, and that patients with lung metastasis who underwent surgical removal of the primary tumor had a better prognosis than those who did not.

The study showed a clear selection bias, with Tan et al. ^[12] analyzing the impact of surgery on the prognosis of lung metastasis in gastric cancer. Overall prognosis was poor for patients with lung metastasis, but those with low tumor burden could benefit from surgical removal of the primary tumor. Patients with widespread metastasis did not experience improved survival, and in some cases, surgery may have increased perioperative risks. Comparing single and multiple organ metastasis, patients with isolated lung metastasis had a better prognosis than those with lung and liver/bone multi-organ metastasis. The presence of lymph node involvement was a significant prognostic factor.

2.4. Metastasis to the peritoneum

The SEER database's tumor coding system has inherent limitations, including missed documentation of retroperitoneal (abdominal) metastases. However, several large-scale SEER studies have investigated the clinical patterns of retroperitoneal metastasis in gastric cancer. Retroperitoneal metastasis is one of the most common patterns of metastasis in gastric cancer. SEER research shows that most patients with retroperitoneal metastasis also have advanced stages of T and N staging. Patients with peritoneal metastasis alone do better than those with peritoneal plus distant organ metastasis. The extent of spread therefore has a strong effect on

outcome. Primary tumor resection provides survival benefit only in certain subgroups. Kaplan-Meier curves can help predict survival and assess the possible benefit of surgery, which may aid patient selection.

Zhang et al.^[13] developed a competing risk skyline plot from SEER. Age, T stage, N stage, tumor grade, surgery and chemotherapy were included. The model was designed to identify patients with peritoneal metastasis who might be suitable for active anticancer treatment. Prognosis was highly heterogeneous. Not all patients with peritoneal metastasis should receive palliative care only. The model can separate those who may benefit from active treatment from those who need supportive care alone. This may reduce a one-size-fits-all approach to clinical decisions.

2.5. Brain metastasis

Brain metastasis is rare in gastric cancer. SEER data show that isolated brain metastasis is very uncommon. Most patients also have liver, lung and bone metastases. Advanced age, high T/N stage, and poorly differentiated tumors increase the risk of brain metastasis. Overall survival rates are very poor after brain metastasis in gastric cancer, with most patients surviving for less than 6 months. Lai et al.^[14] analyzed the relationship between brain metastasis and HER2 expression in gastric cancer using SEER data and external clinical cohorts. Their findings suggest that HER2-positive gastric cancer is associated with a higher risk of brain metastasis, and HER2 status influences the prognosis of patients with brain metastasis. However, the SEER database does not include HER2 molecular markers, and these findings require validation with external cohorts. Compared to other organ-specific metastases, gastric cancer with brain metastasis has the worst prognosis, and the mortality rate further increases when combined with metastases in other organs.

3. Heterogeneity of prognosis in single vs. multiple organ metastasis

Several SEER cohorts show that stage IV gastric cancer is not one prognostic entity. After adjustment for T and N category, the site and number of metastatic organs still separate patients into groups with clearly different survival. Single-organ involvement generally does better than multi-organ involvement. Generally, single-organ metastasis has a better prognosis than multiple-organ metastasis. The survival rates for single-organ metastasis roughly follow the order: peritoneal metastasis > solitary liver metastasis > solitary bone metastasis > solitary brain metastasis. Despite being single-organ metastases, significant differences in survival outcomes were observed between different target organs. Multiple organ metastasis has a significantly worse prognosis compared to any single organ metastasis group. The number of metastatic organs, type of metastatic organ, age, T/N staging, and treatment modality were all independent prognostic factors. Compared to traditional TNM staging, the SEER-derived survival curve provides a more effective method for distinguishing prognosis in Stage IV gastric cancer.

The anatomical location of the primary tumor determines the preferred site of metastasis in gastric cancer. Wang^[15] found, using the SEER database and a domestic single-center registry, that gastric cancer tumors in the lower esophagus have a higher risk of metastasis to the liver, while tumors in the distal stomach have a higher risk of metastasis to the peritoneum. The anatomical location of the primary tumor directly influences the preferred site of distant metastasis, providing a reference for developing pre-operative staging schemes. Liu et al.^[16]'s retrospective study also confirmed that gastric cancer patients in the IV stage exhibit significant differences in survival rates depending on the site of metastasis. Therefore, the site of metastasis should be included in the risk assessment framework for late-stage gastric cancer.

4. Specific tumor subtypes and their organ-specific metastatic characteristics

4.1. Early-stage and late-stage gastric cancer

Wang et al. ^[17] reviewed SEER data across different populations and compared distant metastasis patterns in early-stage and late-stage gastric cancer. Early-stage gastric cancer was more likely to show multi-organ distant metastasis, with a higher incidence of liver and bone metastasis. However, the incidence of purely peritoneal metastasis did not differ clearly between the two groups. Once distant metastasis occurred, early-stage gastric cancer had a worse prognosis. Wu et al. ^[18] reported similar results. Younger patients had a higher risk of liver and bone metastasis, while older patients had a relatively higher proportion of lung metastasis. Differences in pathological subtype distribution were an important source of heterogeneity in metastatic patterns. Bi et al. ^[19] analyzed risk factors for distant metastasis after surgery in early-stage gastric cancer. They emphasized that hidden distant metastasis can exist even in patients with early tumor stages. This supports the need for comprehensive whole-body staging to avoid missing distant disease.

4.2. Gastric G-C cell carcinoma

SEER research indicates that gastric G-C cell carcinoma mainly spreads to the peritoneum, with an increased risk of liver and bone metastasis. Distant metastasis in this subtype is associated with a much poorer prognosis than in non-G-C cell gastric cancer. Depth of tumor invasion, lymph node status, and age are independent risk factors for distant metastasis. Huang et al. ^[20] developed a personalized prediction tool based on SEER data and confirmed that survival differs markedly among G-C cell gastric cancer patients. Wang et al. ^[21] developed a decision tree model for predicting lymph node metastasis risk in G-C cell gastric cancer. Their findings indicated that lymph node positivity serves as an important predisposing factor for both peritoneal and liver metastasis, with affected patients facing a markedly elevated risk of distant metastasis.

4.3. Distant metastasis in early-stage gastric cancer

SEER Data Analysis: Early-stage gastric cancer (T1/T2) primarily involves lymph node metastasis, but distant organ metastasis is still possible. Chen et al. ^[22] developed a predictive model for lymph node-negative, superficial gastric cancer. Even in cases of superficial gastric cancer with negative lymph nodes, metastasis to the liver and lungs can occur, although the incidence is low. However, once distant metastasis occurs, the prognosis for patients with early-stage gastric cancer is poor. Li et al. ^[23] confirmed that lymph node metastasis is a significant predisposing factor for liver, peritoneal, and bone metastasis in early-stage gastric cancer. SEER data show a small number of cT1N0M1 cases where the primary tumor is superficial but has already metastasized. Low-grade, signet ring cell tumors are considered high-risk factors, highlighting the need to be vigilant for hidden distant metastasis, even in superficial tumors.

5. Transfer risks from the SEER database and prognostic prediction models

Recent work has focused on SEER-based decision trees, web-based calculators, and machine learning models. These tools aim to provide individualized predictions of gastric cancer metastasis risk and survival. Wang et al. ^[24] developed a machine learning web calculator for T2–T4 gastric cancer. It assessed the risk of metastasis to the liver, lungs, bones, and peritoneum. The core variables were T stage, N stage, tumor grade, and primary site. The model showed good discrimination. Qin et al. ^[25] found that the weights of risk factors differed by target organ. Liver metastasis was most influenced by N stage, while peritoneal metastasis

was most influenced by tumor differentiation and the presence of mucin-producing cells. Dong et al.^[26] conducted a large SEER analysis of metastasis patterns. They confirmed that the type of metastasis and the number of metastatic sites were independent prognostic factors. These variables can be used as model inputs and may help overcome the limits of traditional TNM staging in stratifying stage IV gastric cancer.

6. Limitations of SEER database research

SEER is a cancer registry database for the US population. Its data on race, etiology, screening methods, and clinical treatment strategies differ from those in China. Any survival curves or machine learning models trained on SEER data should undergo external validation in multiple Chinese centers before they are applied to Chinese patients. The database itself has several limitations. It lacks data on molecular subtypes such as HER2 and MSI. It does not include detailed records of chemotherapy and targeted therapy. Descriptions of abdominal metastasis are incomplete, which can lead to under-recording. Important clinical and pathological information, such as vascular involvement, perineural invasion, and performance status, is often missing. In addition, SEER is a retrospective registry. It can reveal correlations between variables, but it cannot establish causal relationships. Conclusions drawn from SEER data therefore require further validation through prospective studies.

7. Summary and future directions

A large-scale retrospective study based on the SEER database reveals significant heterogeneity in the sites of distant metastasis following gastric cancer. Liver metastasis is the most common form of hematogenous spread, while peritoneal metastasis is the most frequent type of local recurrence; brain metastasis is the rarest and carries the worst prognosis. The type of target organ and the number of metastatic sites are independent prognostic factors, and stage IV gastric cancer should be further stratified.

The primary tumor site, age, and pathological subtype all influence metastatic patterns. Lymph node involvement is a major risk factor for distant metastasis, even in early-stage gastric cancer. Many nomograms and machine learning models are now available for predicting metastasis risk and prognosis. However, these models are limited by the racial composition and coding limits of SEER. They should not be applied directly to other populations without external validation.

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References

- [1] Huang T, Zhuang H, Dai S, et al., 2024, Nomogram Predicting Survival of Patients With Liver Metastasis From Gastric Signet Ring-Cell Carcinoma: A SEER-Based Population Study. *Asian Journal of Surgery*, 47(3): 1669–1672.
- [2] An W, Bao L, Wang C, et al., 2023, Analysis of Related Risk Factors and Prognostic Factors of Gastric Cancer With Liver Metastasis: A SEER and External Validation Based Study. *International Journal of General Medicine*, 16: 5969–5978.
- [3] Li B, Yu J, Zhang Y, et al., 2026, Development and Validation of a Nomogram to Predict Liver Metastases in Patients With Gastric Cancer. *Indian Journal of Surgical Oncology*, 17(6): 1446–1457.
- [4] Wu Y, Guo Y, Luo W, 2024, Prediction of All-Cause Death and Specific Causes of Death in Patients With Gastric Cancer With Liver Metastasis: A Surveillance, Epidemiology, and End Results-Based Study. *Journal of Gastrointestinal Surgery*, 28(6): 880–888.
- [5] Su R, Sun X, Chen S, et al., 2024, Development and Validation of a Nomogram to Predict the Survival and Estimate Surgical Benefits for Gastric Cancer With Liver Metastasis Receiving Primary Tumor Resection. *Frontiers in Oncology*, 14: 1418548.
- [6] Wang Z, Jia X, Yang Y, et al., 2024, Machine Learning-Based Dynamic Predictive Models for Prognosis and Treatment Decisions in Patients With Liver Metastases From Gastric Cancer. *American Journal of Cancer Research*, 14(11): 5521–5538.
- [7] Ji NN, Wu XW, Cao Q, et al., 2024, Influence of Cancer-Directed Surgery on the Prognosis of Liver Metastases From Gastric Cancer. *Clinical and Translational Oncology*, 26(3): 756–764.
- [8] Ren S, Wei Y, Liu W, et al., 2025, Clinical Characteristics, Prognostic Factors and Therapeutic Strategies in Gastric Cancer Patients With Bone Metastasis: A Retrospective Analysis. *Cancer Medicine*, 14(6): e70781.
- [9] Liu B, Li K, Ma R, et al., 2023, Two Web-Based Dynamic Prediction Models for the Diagnosis and Prognosis of Gastric Cancer With Bone Metastases: Evidence From the SEER Database. *Frontiers in Endocrinology*, 14: 1136089.
- [10] Lin Z, Wang R, Zhou Y, et al., 2022, Prediction of Distant Metastasis and Survival Prediction of Gastric Cancer Patients With Metastasis to the Liver, Lung, Bone, and Brain: Research Based on the SEER Database. *Annals of Translational Medicine*, 10(1): 16.
- [11] Zheng H, Li Z, Li J, et al., 2021, Construction, Validation, and Visualization of Two Web-Based Nomograms to Predict Overall and Cancer-Specific Survival in Patients With Gastric Cancer and Lung Metastases. *Journal of Oncology*, 2021: 5495267.
- [12] Tan Z, Du X, Zeng M, et al., 2025, Impact of Cancer-Directed Surgery for Gastric Cancer Patients With Lung Metastasis: A Prognosis Analysis. *Journal of Gastrointestinal Oncology*, 16(3): 890–898.
- [13] Zhang Z, Lu C, Wang W, et al., 2026, Construction of Competing-Risk Nomograms and Identification of Optimal Candidates for Aggressive Therapy in Gastric Cancer With Peritoneal Metastasis: A Population-Based Study. *Translational Cancer Research*, 15(3): 161.
- [14] Lai MY, Guan WL, Yang J, et al., 2024, The Relationship Between Brain Metastasis and HER2 Expression Status in Gastric Cancer. *Clinical and Translational Oncology*, 26(3): 765–773.
- [15] Wang L, Liang B, Jiang Y, et al., 2023, Subsite-Specific Metastatic Organotropism and Risk in Gastric Cancer: A Population-Based Cohort Study of the US SEER Database and a Chinese Single-Institutional Registry. *Cancer Medicine*, 12(19): 19595–19606.

- [16] Liu G, Gu J, Wang J, et al., 2025, Prognostic Implications of Organ-Specific Metastases in Advanced Gastric Cancer: A Retrospective Observational Analysis of the SEER Database. *Medicine*, 104(44): e45570.
- [17] Wang Y, Yin K, Liu D, et al., 2025, Prognosis and Distant Metastasis Patterns of Early-Onset Gastric Cancer Compared With Late-Onset: A Large-Scale, Cross-Population Retrospective Study. *Journal of Gastrointestinal Surgery*, 29(9): 102148.
- [18] Wu F, Wu S, Shuai S, 2024, Distinct Characteristics of Distant Metastasis in Early-Onset Gastric Cancer Patients Compared to Late-Onset Patients: An Observational Study. *Medicine*, 103(20): e38098.
- [19] Bi B, Deng GF, Duan YM, et al., 2023, Retrospective Analysis of Risk Factors for Distant Metastasis of Early-Onset Gastric Cancer During the Perioperative Period. *Frontiers in Oncology*, 13: 1003977.
- [20] Huang D, Li X, Huang Y, et al., 2025, Individualized Prediction Tool for Patients With Metastatic Gastric Signet Cell Carcinoma. *Scientific Reports*, 15(1): 33163.
- [21] Wang W, Xia Y, He C, 2023, Development and Validation of a Predictive Model Associated With Lymph Node Metastasis of Gastric Signet Ring Carcinoma Patients. *Medicine*, 102(45): e36002.
- [22] Chen J, Wu L, Zhang Z, et al., 2021, A Clinical Model to Predict Distant Metastasis in Patients With Superficial Gastric Cancer With Negative Lymph Node Metastasis and a Survival Analysis for Patients With Metastasis. *Cancer Medicine*, 10(3): 944–955.
- [23] Li J, Cui T, Huang Z, et al., 2023, Analysis of Risk Factors for Lymph Node Metastasis and Prognosis Study in Patients With Early Gastric Cancer: A SEER Data-Based Study. *Frontiers in Oncology*, 13: 1062142.
- [24] Wang H, Zhang H, Ma X, et al., 2026, Application of Machine Learning Algorithms and Establishment of a Web Calculator in Predicting Distant Metastasis of T2–T4 Gastric Cancer. *European Journal of Surgical Oncology*, 52(1): 111170.
- [25] Qin X, Qiu B, Ge L, et al., 2024, Applying Machine Learning Techniques to Predict the Risk of Distant Metastasis From Gastric Cancer: A Real-World Retrospective Study. *Frontiers in Oncology*, 14: 1455914.
- [26] Dong Q, Huang M, Lai X, 2024, Metastasis Patterns and Prognosis in Patients With Gastric Cancer: A Surveillance, Epidemiology, and End Results-Based Analysis. *Journal of Gastrointestinal Oncology*, 15(5): 2079–2087.

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