ORIGINAL ARTICLE

# Survival Outcomes of Gastric Adenocarcinoma Patients with Peritoneal Carcinomatosis: A Retrospective Study

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**Background:** Gastric adenocarcinoma is a leading cause of cancer-related mortality worldwide, with peritoneal carcinomatosis representing a critical factor for poor prognosis. The survival of patients with gastric cancer and peritoneal metastasis remains limited, prompting a need for comprehensive studies that explore factors influencing outcomes and potential therapeutic strategies.

**Objective:** To investigate the survival rates and associated prognostic factors of peritoneal carcinomatosis in patients with gastric adenocarcinoma, focusing on the impact of various clinical and pathological characteristics.

**Materials and Methods:** The present study was conducted at Ramathibodi Hospital, Mahidol University, Bangkok, between January 2012 and January 2023. This single-center retrospective study included 106 patients diagnosed with gastric adenocarcinoma and peritoneal metastasis. Data on demographics, clinical presentation, treatment modalities, and outcomes were analyzed. Survival outcomes were assessed using Kaplan-Meier estimated, and factors associated with peritoneal recurrence and survival were identified through logistic regression analysis.

**Results:** The clinical characteristics of 106 patients with gastric cancer and peritoneal metastasis were evaluated. Factors associated with peritoneal recurrence included N stage, lymph node involvement, and the presence of signet ring cells. Patients with positive lymph nodes during the operation were statistically significantly found to be in stage IV group and have peritoneal carcinomatosis recurrence (p=0.007). Furthermore, N stage was associated with recurrence (p=0.027). Survival in patients with gastric adenocarcinoma with peritoneal carcinomatosis who had positive cytology, but negative peritoneal metastasis had median survival time of 5.41 months. Patients with positive malignancy in cytology exam, but positive peritoneal metastasis had median survival time of 5.18 months.

**Conclusion:** Peritoneal metastasis in gastric adenocarcinoma patients is associated with a dismal prognosis. The findings showed the critical need for early detection and the exploration of novel therapeutic strategies. Further research is essential to validate these results and optimize treatment protocols.

**Keywords:** Peritoneal carcinomatosis; Gastric adenocarcinoma; Peritoneal metastasis

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About 20% of all patients diagnosed with gastric cancer present with peritoneal metastasis. Fifty percent of gastric cancer patients undergoing curative resection will later develop peritoneal metastasis. Patients with gastric cancer with peritoneal metastasis have bad prognosis and a median survival of three to six months[1]. Intraabdominal peritoneal metastasis pathophysiology happens when tumor cells dislodge from the gastric cancer, penetrate through the serosa layer, and are able to survive in the peritoneum environment, then adhere to the mesothelial cell layer. The invasion process for the tumor to the sub mesothelial space then appears to be peritoneal metastasis[2].

Recurrent gastric cancer can present with local or distant recurrence, which are peritoneal metastasis. Gastric cancer metastasizes as hematogenous spread and peritoneal metastasis. In the study from Shin et al., in 1,299 patients, it was found that 182 patients had early recurrence in the first two years and 74 patients presented with peritoneal metastasis, which accounted for at least 40% compared to other organ site distant recurrence[3]. Lee et al. studied 245 patients with gastric cancer and peritoneal metastasis. Factors that are associated with such presentation are T3 tumor staging, lymph node metastasis N3, Bormann type 4, infiltrative type cancer, and lymphovascular invasion[4]. According to Koemans et al. study factors related with peritoneal metastasis in gastric

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cancer are non-cardia located tumor, age less than 45 years old, female, gastric cancer T stage T2 to T4, more than one distant metastasis, and diffuse type histology according to Lauren classification[5]. In a meta-analysis from Guan et al., the related factor to peritoneal metastasis from primary gastric cancer are T4 staging tumor, N2/3 stage lymph node metastasis, poor differentiate gastric adenocarcinoma, Bormann type IV gastric adenocarcinoma, tumor size of primary gastric cancer larger than 4 cm, CA 125 of 35 ng/mL or more, CA 199 of 37 ng/mL or more, diffuse type gastric cancer according to Lauren classification, and presence of signet ring cell in histopathology[6].

The diagnostic imaging modality in peritoneal metastasis gastric adenocarcinoma is the computed tomography. It is the most used as the first modality because the staging diagnosis is mandatory. Findings that suggest peritoneal metastasis are ascites, omental nodule, or omental cake. Computed tomography has low specificity. Computed tomography can detect lesions of peritoneal metastasis of 1 cm, which makes it a low sensitivity method. According to the positron emission tomography scan, the computed tomography has low sensitivity in detecting peritoneal metastasis and may need other adjunctive investigation[7]. The other method is magnetic resonance imaging (MRI), which can detect peritoneal lesions having a minimum width of 5 mm, which can be seen on diffusion-weighted imaging (DWI)-MRI phase. However, MRI is commonly used to detect peritoneal metastasis in ovarian cancer or appendiceal cancer. Other beneficial use of MRI is to use in monitoring if the peritoneal metastasis responds to treatment[8]. Computed tomography colonography can also detect peritoneal metastasis according to Iwasaki et al[9]. Eighteen patients that had gastric cancer with peritoneal metastasis underwent computed tomography colonography. The sensitivity was 83.3% and specificity was 100%.

One of the methods to diagnose peritoneal metastasis according to guidelines suggest performing a laparoscopy diagnosis and cytology examination in patients with T stage 1Tb and onwards to get the accurate staging and give the most appropriate management. Staging laparoscopies can help identify disseminated nodules that could not be diagnosed with imaging. Detection rate of laparoscopic method is 47% to 51.6%[10]. Cytology examination can be done by peritoneal lavage, which is done, even without visible peritoneal nodules. Cytology examination can increase detection by 13.2% for positive malignancy result. When combining laparoscopic diagnosis with a peritoneal lavage cytology, it can detect peritoneal metastasis in 36%[11].

The aim of treating gastric cancer with peritoneal metastasis is as a systemic therapy approach and offering palliative care. The innovation of targeted therapy and immunotherapy provide longer survival time. In the study from Yamaguchi et al.[12], a conversion therapy in gastric cancer with metastasis patients was done by giving preoperative systemic treatment that may convert patients to curative intent, which included patients that were cytology positive or had peritoneal nodules. Hyperthermic intraperitoneal chemotherapy (HIPEC) has been studied for prophylaxis treatment[13]. In the study from Coccolini et al., they studied the survival in gastric patients who underwent curative surgery and got prophylaxis HIPEC or none. This group of T3 and T4 patients showed that patients who underwent prophylactic HIPEC had disease-free survival of about 34.5 months in T3 and 35.6 months in T4, respectively. While patients without prophylactic HIPEC had shorter disease-free survival at 27.7 months in T3 and 21.6 months in T4[14]. From the meta-analysis of Zhuang et al. prophylaxis HIPEC helped decrease peritoneal metastasis in high-risk gastric cancer patients. Peritoneal recurrence rate in 973 patients was favorable in prophylactic HIPEC group with odd ration of 0.24 (95% CI 0.13 to 0.42)[15].

The present research was to study the survival in patients with gastric cancer with peritoneal metastasis in terms of positive cytology or positive peritoneal metastasis from imaging or tissue diagnosis or both in Ramathibodi Hospital. Secondary outcome was to study the factors associated with the peritoneal recurrence of gastric cancer. This information might help guide the treatment to these patients with the aim of lengthening survival.

## Material and Methods

### Population

One hundred six patients diagnosed as gastric adenocarcinoma with peritoneal metastasis in Ramathibodi Hospital, Mahidol University, Bangkok, between January 2012 and January 2023 were included in this study. Inclusion criteria included patients with gastric adenocarcinoma diagnosed with gastroduodenoscopy or surgery with pathological information of adenocarcinoma of stomach and have synchronous or metachronous peritoneal metastasis.

### Study design

All patients who had gastric adenocarcinoma with

synchronous and metachronous peritoneal metastasis were included in this study. Patients who were attempted for curative subtotal or total gastrectomy according to location of tumor were also included. The definition of surgery was done according to the Japanese Gastric Cancer guideline. Pathological results from biopsy gastroduodenoscopy were evaluated in accordance with Lauren classification, tumor differentiation, present of signet ring cell, and present of poor cohesive cell. These included pathological results from major surgery and evaluation of tumor size, tumor differentiation, presence of signet ring cell or poor cohesive cell, presence of lymphovascular invasion or perineural invasion, metastatic of regional lymph node, tumor staging, lymph node staging, and completion of resection. Cytological examination was obtained from abdominal fluid tapping or peritoneal washing from surgery in curative setting or laparoscopic diagnosis. Patients with peritoneal metastasis were diagnosed with gross peritoneal nodules, presence of peritoneal nodules/findings on computer tomography scan, or pathological result of peritoneal biopsy. Patients in the present study may have received chemotherapy in neoadjuvant, adjuvant, or palliative aim. The medical records and computerized records of patients were collected. The follow-up data were from the medical records, follow up medical oncologist, or surgical oncologist physician.

### Statistical analysis

Stata, version 15.1 Licensed (StataCorp LP, College Station, TX, USA) were used for data analysis. Clinicopathological information characteristic of patients showing the proportion of information in each group was stratified. Continuous data is presented as average and standard deviation or median and quartile range. Risk factors for recurrence analyzed by logistic regression analysis were applied to identify factors associated with recurrence. The results of the statistical tests were significant when the p-value was less than 0.05. The overall survival of patients according to cytological examination results are presented in Kaplan-Meier survival estimations.

### Ethics approval

The present study was approved by the Ethics Committee of Faculty of Medicine Ramathibodi Hospital, Mahidol University (No. MURA2023/464).

## Results

Table 1 presents the clinical characteristics of 106 patients with gastric cancer and peritoneal metastasis. There were 36 male and 70 female patients. The average age of the patients who underwent surgery for primary gastric cancer was 63 years old, those who had not undergone surgery was 55.9 years old. The average tumor size in patients who underwent surgery was 7.55 cm. according to maximal diameter of pathological specimen. Most of the patients had tumor located at gastric antrum and the second most common located at the body of stomach. Most of the patients' tissue biopsied showed diffuse type according to Lauren classification. The patients who underwent surgery for treatment as gastrectomy had lymphatic invasion in 91.3%, vascular invasion in 91.3%, and perineural invasion in 44 patients (95.65%). The main tumor differentiation in gastric cancer among study population was poor differentiation in patients who undergone surgery was 42 patients (89.36%) and in the non-surgery group was 41 patients (87.23%). Pathological staging in patients who underwent surgery had clinical T4 stage in 52.17% and T3 in 41.3%, including pathological N3 lymph node was found in 31 patients (65.96%). Forty-seven patients (79.66%) with gastric cancer and peritoneal carcinomatosis had chemotherapy without surgery while 40 patients (85.11%) underwent surgery.

Table 2 is stratified by death in patients with gastric adenocarcinoma and peritoneal metastasis. Tumor size in both dead and alive patients was similar, which was 7.49 cm in alive patients and 7.45 cm in dead patients. Most of the tumors were located in antrum on both dead and alive patients. The dead patients were diagnosed with diffuse Lauren classification type in 69.57% of the cases. Patients who were still alive were found to have no lymphatic invasion in 13.04%, compared to dead patients who had no lymphatic and vascular invasion in 7.41%. Twenty-five patients (96.30%) had lymphatic invasion in dead patients. Patients in both dead and alive groups were similar in having perineural invasion with 22 patients (95.65%) who were still alive and 26 patients (96.3%) who were dead. Thirty-three patients (75%) alive patients and 44 (88%) dead patients had tumor differentiation. Moderately differentiated tumors were found proportionally more in the alive patients with 11 (25%) than in the dead patients with five (10%). Positive for malignancy lymph nodes after surgery in gastric cancer in alive patients was 20 (40.83%) and dead patients was 24 (42.11%). The alive patients who had stage T3 tumors were 12 (48%) and T4 were 10 (40%), while in the

**Table 1.** Clinicopathological characteristics stratified by surgery of primary tumor

| Characteristics | | Primary tumor surgery (n=106) | | p-value | Univariable logistic regression | | p-value |
|---|---|---|---|---|---|---|---|
| | | No (n=59) | Yes (n=47) | | OR | 95% CI | |
| Sex; n (%) | Male | 22 (37.29) | 14 (29.79) | 0.418 | | | |
| | Female | 37 (62.71) | 33 (70.21) | | | | |
| Age at diagnostic GC (years); mean [SD] | | 55.91 [11.66] | 63.59 [13.58] | 0.002* | 1.05 | 1.01 to 1.08 | 0.003 |
| Tumor size (cm); mean [SD] | | | 7.55 [3.59] | 0.62 | | | |
| Tumor location; n (%) | Antrum | 26 (44.07) | 25 (53.19) | 0.042* | Ref. | Ref. | Ref. |
| | Body | 15 (25.42) | 14 (29.79) | | 0.97 | 0.38 to 2.41 | 0.949 |
| | Cardia | 4 (6.78) | 6 (12.77) | | 1.56 | 0.39 to 6.19 | 0.527 |
| | Fundus | 6 (10.17) | 2 (4.26) | | 0.34 | 0.06 to 1.88 | 0.220 |
| | Diffuse | 8 (13.56) | 0 (0.00) | | - | - | - |
| Lauren classification; n (%) | Diffuse type | 7 (63.64) | 18 (62.07) | 0.834 | | | |
| | Intestinal type | 3 (27.27) | 5 (17.24) | | | | |
| | Mucinous type | 0 (0.00) | 1 (3.45) | | | | |
| | Mix type | 1 (9.09) | 5 (17.24) | | | | |
| Lymphatic invasion; n (%) | Positive | | 42 (91.30) | | | | |
| | Negative | | 4 (8.70) | | | | |
| Vascular invasion; n (%) | Positive | | 42 (91.30) | | | | |
| | Negative | | 4 (8.70) | | | | |
| Perineural invasion; n (%) | Positive | | 44 (95.65) | | | | |
| | Negative | | 2 (4.35) | | | | |
| Pathologic result; n (%) | SRC | 24 (41.38) | 23 (48.94) | 0.020* | 1.91 | 0.83 to 4.39 | 0.124 |
| | PCH | 2 (3.45) | 8 (17.02) | | 8 | 1.51 to 42.14 | 0.014 |
| | None | 32 (55.17) | 16 (34.04) | | Ref. | Ref. | Ref. |
| Tumor differentiation; n (%) | Poor differentiate | 41 (87.23) | 36 (76.60) | 0.169 | | | |
| | Moderate differentiate | 5 (10.64) | 11 (23.40) | | | | |
| | Well differentiate | 1 (2.13) | 0 (0.00) | | | | |
| Lymph node; n (%) | Positive | | 42 (89.36) | 0.001* | 8.4 | 0.96 to 73.43 | 0.054 |
| | Negative | | 5 (10.64) | | Ref. | Ref. | Ref. |
| | Not retrieved | | 0 (0.00) | | - | - | - |
| T stage; n (%) | T1 | | 0 (0.00) | 0.999 | | | |
| | T2 | | 3 (6.52) | | | | |
| | T3 | | 19 (41.30) | | | | |
| | T4 | | 24 (52.17) | | | | |
| N stage; n (%) | N0 | | 4 (8.51) | 0.001* | Ref. | Ref. | Ref. |
| | N1 | | 2 (4.26) | | - | - | - |
| | N2 | | 8 (17.02) | | 4 | 0.27 to 58.56 | 0.311 |
| | N3 | | 31 (65.96) | | 15.5 | 1.13 to 212.1 | 0.040 |
| | Not retrieved | | 2 (4.26) | | - | - | - |
| Resection; n (%) | R0 | | 28 (59.57) | 0.001* | Ref. | Ref. | Ref. |
| | R1 | | 16 (34.04) | | - | - | - |
| | R2 | | 1 (2.13) | | - | - | - |
| | No surgery | | 2 (4.26) | | 0.005 | 0.001 to 0.03 | 0.001 |
| Chemotherapy; n (%) | Yes | 47 (79.66) | 40 (85.11) | 0.612 | | | |
| | No | 12 (20.34) | 7 (14.89) | | | | |

GC=gastric cancer; SRC=signet ring cell carcinoma; PCH=poorly cohesive carcinoma; SD=standard deviation; OR=odds ratio; CI=confidence interval
* Statistical significance

dead patients, 11 (37.93%) had T3 and 18 (52.63%) had T4 tumors. In the alive patients, two patients (4.08%) had N1, three (6.12%) had lymph node N2, and 14 (28.57%) had N3. The dead patients, none had N1, but six (10.53%) had N2, and 18 (31.58%) had N3. Chemotherapy was administered in both alive and dead patients.

Patients who first presented with peritoneal

**Table 2.** Clinicopathological characteristics stratified by death in gastric adenocarcinoma with peritoneal metastasis

| Characteristics | | Dead (n=106) | | p-value |
|---|---|---|---|---|
| | | No (n=49) | Yes (n=57) | |
| Sex; n (%) | Male | 17 (34.69) | 19 (33.33) | 0.883 |
| | Female | 32 (65.31) | 38 (66.67) | |
| Age at diagnostic GC (years); mean [SD] | | 61.06 [12.41] | 57.82 [13.52] | 0.205 |
| Tumor size (cm); mean [SD] | | 7.49 [3.90] | 7.45 [3.24] | 0.966 |
| Tumor location; n (%) | Antrum | 24 (48.98) | 27 (47.37) | 0.101 |
| | Body | 15 (30.61) | 14 (24.56) | |
| | Cardia | 3 (6.12) | 7 (12.28) | |
| | Fundus | 1 (2.04) | 7 (12.28) | |
| | Diffuse | 6 (12.24) | 2 (3.51) | |
| Lauren classification; n (%) | Diffuse type | 9 (52.94) | 16 (69.57) | 0.061 |
| | Intestinal type | 6 (35.29) | 2 (8.70) | |
| | Mucinous type | 1 (5.88) | 0 (0.00) | |
| | Mix type | 1 (5.88) | 5 (21.74) | |
| Lymphatic invasion; n (%) | Positive | 20 (86.96) | 25 (92.59) | 0.651 |
| | Negative | 3 (13.04) | 2 (7.41) | |
| Vascular invasion; n (%) | Positive | 20 (86.96) | 25 (92.59) | 0.951 |
| | Negative | 3 (13.04) | 2 (7.41) | |
| Perineural invasion; n (%) | Positive | 22 (95.65) | 26 (96.30) | 0.999 |
| | Negative | 1 (4.35) | 1 (3.70) | |
| Pathological result; n (%) | SRC | 21 (43.75) | 26 (45.61) | 0.176 |
| | PCH | 2 (4.17) | 8 (14.04) | |
| | None | 25 (52.08) | 23 (40.35) | |
| Tumor differentiation; n (%) | Poor differentiation | 33 (75.00) | 44 (88.00) | 0.108 |
| | Moderate differentiation | 11 (25.00) | 5 (10.00) | |
| | Well differentiation | 0 (0.00) | 1 (2.00) | |
| Lymph node; n (%) | Positive | 20 (40.82) | 24 (42.11) | 0.836 |
| | Negative | 4 (8.16) | 3 (5.26) | |
| | Not retrieved | 25 (51.02) | 30 (52.63) | |
| T stage; n (%) | T1 | - | - | |
| | T2 | 3 (12.00) | 0 (0.00) | 0.080 |
| | T3 | 12 (48.00) | 11 (37.93) | |
| | T4 | 10 (40.00) | 18 (62.07) | |
| N stage; n (%) | N0 | 4 (8.16) | 2 (3.51) | 0.475 |
| | N1 | 2 (4.08) | 0 (0.00) | |
| | N2 | 3 (6.12) | 6 (10.53) | |
| | N3 | 14 (28.57) | 18 (31.58) | |
| | Not retrieved | 26 (53.06) | 31 (54.39) | |
| Resection; n (%) | R0 | 15 (30.61) | 17 (29.82) | 0.639 |
| | R1 | 6 (12.24) | 10 (17.54) | |
| | R2 | 1 (2.04) | 0 (0.00) | |
| | No surgery | 27 (55.10) | 30 (52.63) | |
| Chemotherapy; n (%) | Yes | 38 (77.55) | 49 (85.96) | 0.260 |
| | No | 11 (22.45) | 8 (14.04) | |

GC=gastric cancer; SRC=signet ring cell carcinoma; PCH=poorly cohesive carcinoma; SD=standard deviation

* Statistical significance

metastasis in gastric adenocarcinoma were in the non-recurrence group, but the ones that later developed peritoneal metastasis were in the recurrence group.

Table 3 is stratified by gastric adenocarcinoma patients with peritoneal carcinomatosis who presented with recurrence and stage IV. Patients presenting with gastric adenocarcinoma who were diagnosed with peritoneal carcinomatosis at presentation were 58 and

**Table 3.** Clinicopathological characteristics stratified by recurrence

| Characteristics | | Recurrence (n=106) | | p-value | Univariable logistic regression | |
|---|---|---|---|---|---|---|
| | | No (n=58) | Yes (n=48) | | OR | 95% CI |
| Sex; n (%) | Male | 23 (39.66) | 13 (27.08) | 0.174 | | |
| | Female | 35 (60.34) | 35 (72.92) | | | |
| Tumor size (cm); mean [SD] | | 8.15 [3.36] | 6.98 [3.63] | 0.266 | | |
| Tumor location; n (%) | Antrum | 32 (55.17) | 19 (39.58) | 0.137 | | |
| | Body | 11 (18.97) | 18 (37.50) | | | |
| | Cardia | 4 (6.90) | 6 (12.50) | | | |
| | Fundus | 5 (8.62) | 3 (6.25) | | | |
| | Diffuse | 6 (10.34) | 2 (4.17) | | | |
| Lauren classification; n (%) | Diffuse type | 10 (58.82) | 15 (65.22) | 0.603 | | |
| | Intestinal type | 5 (29.41) | 3 (13.04) | | | |
| | Mucinous type | 0 (0.00) | 1 (4.35) | | | |
| | Mix type | 29 (11.76) | 4 (17.39) | | | |
| Lymphatic invasion; n (%) | Positive | 19 (100) | 26 (83.97) | 0.142 | | |
| | Negative | 0 (0.00) | 5 (16.13) | | | |
| Vascular invasion; n (%) | Positive | 19 (100) | 26 (83.87) | 0.142 | | |
| | Negative | 0 (0.00) | 5 (16.13) | | | |
| Perineural invasion; n (%) | Positive | 18 (94.74) | 30 (96.77) | 0.999 | | |
| | Negative | 1 (5.26) | 1 (3.23) | | | |
| Pathological result; n (%) | SRC | 25 (43.10) | 22 (46.81) | 0.442 | | |
| | PCH | 4 (6.90) | 6 (12.77) | | | |
| | None | 29 (50.00) | 19 (40.43) | | | |
| Tumor differentiation; n (%) | Poor differentiation | 42 (84.00) | 35 (79.55) | 0.583 | | |
| | Moderate differentiation | 7 (14.00) | 9 (20.45) | | | |
| | Well differentiation | 1 (2.00) | 0 (0.00) | | | |
| Lymph node; n (%) | Positive | 18 (31.03) | 26 (54.17) | 0.007* | 0.57 | 0.10 to 3.31 |
| | Negative | 2 (3.45) | 5 (10.42) | | Ref. | Ref. |
| | Not retrieved | 38 (65.52) | 17 (35.42) | | - | - |
| T stage; n (%) | T1 | - | - | | | |
| | T2 | 2 (9.52) | 1 (3.03) | 0.726 | | |
| | T3 | 9 (42.86) | 14 (42.42) | | | |
| | T4 | 10 (47.62) | 18 (54.55) | | | |
| N stage; n (%) | N0 | 2 (3.45) | 4 (8.33) | 0.027* | Ref. | Ref. |
| | N1 | 1 (1.72) | 1 (2.08) | | 0.5 | 0.01 to 12.89 |
| | N2 | 4 (6.90) | 5 (10.42) | | 0.62 | 0.07 to 5.34 |
| | N3 | 12 (20.69) | 20 (41.67) | | 0.83 | 0.13 to 5.25 |
| | Not retrieved | 39 (67.24) | 18 (37.50) | | - | - |
| Resection; n (%) | R0 | 12 (20.69) | 20 (41.67) | 0.010* | Ref. | Ref. |
| | R1 | 7 (12.07) | 9 (18.75) | | 0.77 | 0.22 to 5.61 |
| | R2 | 0 (0.00) | 1 (2.08) | | - | - |
| | No surgery | 39 (67.24) | 18 (37.50) | | - | - |
| Chemotherapy; n (%) | Yes | 47 (81.03) | 40 (83.33) | 0.804 | | |
| | No | 11 (18.97) | 8 (16.67) | | | |

GC=gastric cancer; SRC=signet ring cell carcinoma; PCH=poorly cohesive carcinoma; SD=standard deviation; OR=odds ratio; CI=confidence interval
* Statistical significance

patients who had recurrence were 48. Patients with recurrence occurred in 35 female patients (72.92%) and 35 male patients (60.34%). Patients who did not present with peritoneal carcinomatosis had average tumor size 8.15 cm and patients who presented with peritoneal carcinomatosis had average tumor size 6.98 cm, no significance difference was found (p=0.266). Most patients had tumor located at the antrum in 19 recurrence patients (39.58%) and 32 no recurrence patients (55.17%), no statistical difference

(p=0.137).

According to the histopathological reports, there were no difference statistically in both recurrence group and those presented with peritoneal carcinomatosis for diffuse type (p=0.603), lymphatic invasion (p=0.142), vascular invasion (p=0.142), and perineural invasion (p=0.999). In the patients with peritoneal carcinomatosis recurrence group, 22 patients (46.81%) were found with signet ring cell, six (12.77%) with poorly cohesive, and 19 (40.43%) with non-signet ring cell, and patients with stage IV at presentation, 25 patients (43.10%) with signet ring cell, four (6.90%) with poorly cohesive, and 29 (50%) with non-signet ring cell, but no statistical difference (p=0.442). Patients with positive lymph node on operation were found to have statistical significance in both stage IV group and peritoneal carcinomatosis recurrence (p=0.007). Differences in T stage did not show any significance (p=0.726). However, N stage was associated with recurrence (p=0.027). In recurrence group with N stage, one patient (2.08%) had N1, two (10.42%) had N2, and 20 (41.67%) had N3. Complete resection was found to associate with recurrence (p=0.010).

Chemotherapy was administered in both groups. In the recurrence group, 40 patients (83.33%) underwent chemotherapy and in the stage IV group 47 patients (81.03%) underwent chemotherapy, without any statistical significance (p=0.804).

Table 4 presents the patients who had cytologic exams, which was 59 patients out of 106 patients. The positive cytology group had a higher percentage of females at 57.78% compared to males at 42.22%. However, the difference in gender distribution was not statistically significant (p=0.360). The mean age at diagnosis for the positive cytology group was slightly higher at 60.55 years than the negative cytology group at 56.64 years, but this difference was not statistically significant (p=0.297). Average tumor size did not differ significantly between the positive group at a mean of 7.78 cm and the negative group, who had a mean of 9 cm (p=0.472). The antrum was the most common location for tumors in both the positive, for 46.67%, and the negative, for 42.86%, of the cytology groups. No significant differences were observed in tumor location distributions between the two groups (p=0.196). The diffuse type was more common in the positive cytology group at 72.22%, compared to the negative group at 33.33%. However, the difference in Lauren classification between the groups was not statistically significant (p=0.149). Lymphatic invasion was present in 100% of the positive group and 87.50% of the negative group, with no significant difference (p=0.308). Similarly vascular invasion was observed in all patients of the positive group and 87.50% of the negative group, again not significantly different (p=0.126). Perineural invasion was present in all patients in the positive group and 75% of the negative group. This difference was not statistically significant (p=0.086). No significant difference in the distribution of signet ring cell carcinoma and poorly cohesive carcinoma was observed between the groups (p=0.448), but poor differentiation was predominant in both positive at 84.21% and negative at 84.62% cytology groups with no significant difference (p=0.999). Positive lymph node involvement was slightly more common in the positive cytology group at 37.78% compared to the negative group at 50%, but this difference was not statistically significant (p=0.513). There was no significant difference in N stages, for N0 to N3, between positive and negative cytology groups (p=0.336). The proportion of patients who achieved complete resection (R0) was slightly higher in the positive cytology group at 22.22% compared to the negative group at 42.86%, but this was not statistically significant (p=0.314). A large majority of both groups received chemotherapy, with 71.11% in the negative and 60% in the positive cytology groups, showing no significant difference (p=0.483).

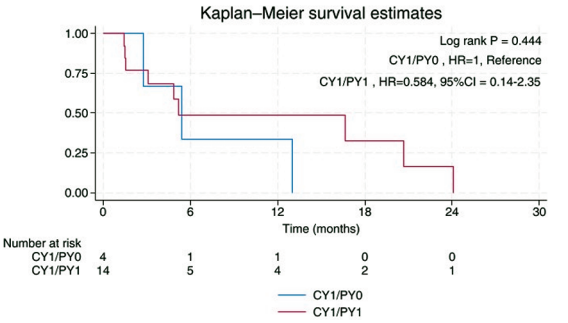


**Figure 1.** Kaplan-Meier estimate for overall survival.

The survival curve in patients with gastric adenocarcinoma with peritoneal carcinomatosis who had positive cytology, but negative peritoneal metastasis had median survival time of 5.41 months. Patients with positive malignancy in cytology exam, but positive peritoneal metastasis had median survival time 5.18 months (Figure 1).

## Discussion

It is widely known that metastatic gastric cancer has poor prognosis. Gastric cancer is the fourth

**Table 4.** Clinicopathological characteristics in gastric adenocarcinoma with peritoneal metastasis who underwent cytologic examination

| Characteristics | | Cytology result (n=59) | | p-value |
|---|---|---|---|---|
| | | Negative (n=14) | Positive (n=45) | |
| Sex; n (%) | Male | 4 (28.57) | 19 (42.22) | 0.360 |
| | Female | 10 (71.43) | 26 (57.78) | |
| Age at diagnostic GC (years); mean [SD] | | 56.64 [14.73] | 60.55 [11.27] | 0.297 |
| Tumor size (cm); mean [SD] | | 9.00 [3.31] | 7.78 [3.88] | 0.472 |
| Tumor location; n (%) | Antrum | 6 (42.86) | 21 (46.67) | 0.196 |
| | Body | 5 (35.71) | 7 (15.56) | |
| | Cardia | 3 (21.43) | 6 (13.33) | |
| | Fundus | 0 (0.00) | 4 (8.89) | |
| | Diffuse | 0 (0.00) | 7 (15.56) | |
| Lauren classification; n (%) | Diffuse type | 2 (33.33) | 13 (72.22) | 0.149 |
| | Intestinal type | 2 (33.33) | 3 (16.67) | |
| | Mucinous type | 1 (16.67) | 0 (0.00) | |
| | Mix type | 1 (16.67) | 2 (11.11) | |
| Lymphatic invasion; n (%) | Positive | 7 (87.50) | 18 (100) | 0.308 |
| | Negative | 1 (12.50) | 0 (0.00) | |
| Vascular invasion; n (%) | Positive | 7 (87.50) | 18 (100) | 0.126 |
| | Negative | 1 (12.50) | 0 (0.00) | |
| Perineural invasion; n (%) | Positive | 6 (75.00) | 18 (100) | 0.086 |
| | Negative | 2 (25.00) | 0 (0.00) | |
| Pathological result; n (%) | SRC | 6 (42.86) | 22 (50.00) | 0.448 |
| | PCH | 2 (14.29) | 2 (4.55) | |
| | None | 6 (42.86) | 20 (45.45) | |
| Tumor differentiation; n (%) | Poor differentiate | 11 (84.62) | 32 (84.21) | 0.999 |
| | Moderate differentiate | 2 (15.38) | 6 (15.79) | |
| | Well differentiate | - | - | |
| Lymph node; n (%) | Positive | 7 (50.00) | 17 (37.78) | 0.513 |
| | Negative | 1 (7.14) | 2 (4.44) | |
| | Not retrieved | 6 (42.86) | 26 (57.78) | |
| T stage; n (%) | T1 | - | - | - |
| | T2 | 1 (12.50) | 1 (4.76) | 0.659 |
| | T3 | 4 (50.00) | 9 (42.86) | |
| | T4 | 3 (37.50) | 11 (52.38) | |
| N stage; n (%) | N0 | 1 (7.14) | 2 (4.44) | 0.336 |
| | N1 | 1 (7.14) | 0 (0.00) | |
| | N2 | 2 (14.29) | 3 (6.67) | |
| | N3 | 4 (28.57) | 14 (31.11) | |
| | Not retrieved | 6 (42.86) | 26 (57.78) | |
| Resection; n (%) | R0 | 4 (28.57) | 10 (22.22) | 0.314 |
| | R1 | 3 (21.43) | 8 (17.78) | |
| | R2 | 1 (7.14) | 0 (0.00) | |
| | No surgery | 6 (42.86) | 27 (60.00) | |
| Chemotherapy; n (%) | Yes | 12 (85.71) | 32 (71.11) | 0.483 |
| | No | 2 (14.29) | 13 (28.89) | |

GC=gastric cancer; SRC=signet ring cell carcinoma; PCH=poorly cohesive carcinoma; SD=standard deviation

* Statistical significance

leading cause of death[16]. Treatments, including both systemic and local treatment, emerged in many ways. The most common sites of metastasis were liver at 48%, peritoneum at 32%, lung at 15%, and bone at 12%. Metastases to lungs, nervous system, and bone were more frequently found in cancer

located at cardia. Peritoneum metastasis was found in non-cardia located cancer, which is often found in signet ring cell histology. Additionally signet ring cell adenocarcinomas frequently metastasized to bone and ovary[17]. In the present study, most of the patients are non-cardia located gastric adenocarcinoma at antrum or body of stomach. The prevalence of gastric cancer in Eastern Asia is higher than western countries, including Japan, Mongolia, and Korea. In which also Asian patients have higher prevalence of gastric cancer located more to the distal part of stomach. The majority of Thai patients with gastric adenocarcinoma are female and mostly present with stage IV, in about 55% of the cases, and most common have poor differentiate and signet ring cell feature[18]. The histopathological tissue results of the patients who had peritoneal metastasis dominantly included signet ring cell features.

Peritoneal metastasis in gastric cancer is one of poor prognosis. In Asia most frequent treatment failure in curative intent is peritoneal dissemination caused by free cancer from primary gastric cancer and median overall survival is three to six months[19]. The patients studied with confirmed CY0/PY1 or CY1/PY1 had a median overall survival for about five months. Some of the patients did not undergo cytology examination due to intra-ops being found with gross peritoneal metastasis and did not undergo peritoneal cytology examination. In the study from Yarema et al. with palliative chemotherapy in patients with diffuse peritoneal metastasis, the overall survival was up to 5.6 months, and in cases of best supportive care, the overall survival was 3.2 months[20]. Other treatment being more developed is intraperitoneal chemotherapy[21]. Intraperitoneal therapeutic method, such as cytoreductive surgery with HIPEC has been proposed. Glehen et al. multi-institutional retrospective study of peritoneal metastasis patients who underwent cytoreductive surgery and HIPEC and/or early postoperative intra-peritoneal chemotherapy had a median overall survival of 9.2 months and 5-year survival rates of 13%[22]. It seems that the future therapeutic treatments, which are better and more developed, would definitely provide better survival. However, there are also other factors contributing to poor prognosis. Patients with gastric adenocarcinoma with peritoneal metastasis have associated factors such as histologic types, T stage, and N stage according to Elkordy et al[23]. In the present study, there were no significant factors that were risk of peritoneal metastasis.

Studies have shown risk factors of peritoneal metastasis in gastric adenocarcinoma. Wu et al. found gastric cancer patients with peritoneal recurrence were associated with deeper depth of invasion at T stage, a greater number of metastatic lymph nodes, lower differentiation, lymphovascular invasion, and perineural invasion[24]. In the present study, there was difference based on lymph node involvement in the recurrence and no recurrence group, but logistic regression suggested that lymph node positivity is not a significant predictor of recurrence. Anyhow, the numbers of lymph nodes involvement associated with peritoneal recurrence and as to the T staging, most of the patients who had peritoneal recurrence have either T3 or T4 stage of primary tumor. The study from Thomassen et al.[25] found that peritoneal metastasis in gastric cancer associated with higher odd ratios of developing peritoneal carcinomatosis in younger than 60 years old patients, female gender, advanced T and N stage, or primary tumor of signet ring cells.

In the present study, there were no associated factors about having positive or negative cytology result in all gastric adenocarcinoma with peritoneal metastasis. The median overall survival of positive cytology with positive or negative peritoneum gross metastasis was similar. The explanation is that with positive metastatic adenocarcinoma has poor prognosis.

While meta-analysis from Jamel et al.[26] demonstrated negative peritoneal cytology before treatment improved survival rate when compared with positive cytology, the negative cytology after neoadjuvant chemotherapy was associated with improved overall survival. However, in the present study, regardless of the cytology result, having peritoneal metastasis had similar median overall survival. Regardless of poor prognosis, conversion therapy is another method for stage IV gastric cancer with negative macroscopic peritoneal dissemination. However, a positive cytology for malignancy can undergo neoadjuvant chemotherapy and primary gastrectomy may prolong survival. From the study of Valletti et al.[27], they observed higher conversion rate to CY negative after treatment with FLOT compared to ECF ($p=0.27$), and conversion to CY negative after neoadjuvant chemotherapy resulted in an improved overall survival. With this concept, patients with positive cytology examination but no evidence of gross peritoneal metastasis disease may benefit from neoadjuvant chemotherapy. Therefore, laparoscopic diagnosis is important as it helps detect patients with peritoneal metastasis, thus avoiding unnecessary

surgery. In addition, patients with positive cytology can be directed to receive chemotherapy beforehand.

The authors' patients diagnosed with peritoneal metastasis have often undergone palliative chemotherapy. Between Thailand and Japan, patients are treated similarly including fluoroucil (5-FU), platinum-based oxaliplatin, or cisplatin[28].

## Limitation

The patients in the present study were underpowered to find significance of the risk factors of peritoneal metastasis in gastric adenocarcinoma. Some patients did not undergo peritoneal cytology examination due to first diagnosed of peritoneal metastasis from imaging investigation or peritoneal nodule biopsy. The variety of treatment or sequence may differ among patients. Furthermore, in earlier years, patients who underwent curative surgery did not receive peritoneal washing.

## Conclusion

Peritoneal metastasis in gastric adenocarcinoma patients is associated with a dismal prognosis, with survival significantly impacted by T stage and lymph node involvement. The median overall survival of positive or negative cytologic examination did not differ with median overall survival of five months when patients had peritoneal metastasis. The findings showed the critical need for early detection and the exploration of novel therapeutic strategies. Laparoscopic diagnosis in gastric cancer plays a crucial role in accurate staging, preventing unnecessary surgery and optimizing treatment by detecting peritoneal metastasis and obtaining cytology that imaging cannot detect. Further research is essential to validate these results and optimize treatment protocols.

## What is already known about this topic?

Gastric cancer is the fourth leading cause of death. Metastatic gastric cancer has poor prognosis. The most common sites of metastasis were liver in 48%, peritoneum in 32%, lung in 15%, and bone in 12%. Patients with gastric cancer with peritoneal metastasis have bad prognosis.

## What does this study add?

The median overall survival of positive or negative cytologic examination did not differ with median overall survival of five months when patients had peritoneal metastasis.

The median overall survival of positive cytology with positive or negative peritoneum gross metastasis was similar.

Factors associated with peritoneal recurrence included T stage, lymph node involvement, and the presence of signet ring cells.


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## Conflicts of interest

The authors declare no conflict of interest.

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