Gastrointestinal metastasis of primary lung cancer: An analysis of 366 cases

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Abstract. The gastrointestinal (GI) tract is not a common site of metastasis in primary lung cancer. The aim of the present study was to reveal the clinical and prognostic characteristics of gastrointestinal metastases of lung cancer (GMLC). Information on 366 cases of GMLC was collected and factors that affect severe GI complications were analyzed. Univariate and multivariate survival analyses were performed using the Cox proportional hazards model. Of the cases analyzed, the small intestine (59.6%) and colorectum (25.6%) were the two organs where lung cancer was most likely to metastasize in the GI tract. Squamous cell carcinoma (28.5%), adenocarcinoma (27.6%) and large cell carcinoma (20.9%) were the three most common histological types. However, compared with the histological distributions of primary lung cancer, patients with large cell carcinoma exhibited the highest elevated risk of GMLC [relative risk (RR), 4.07; P<0.001] and those with adenocarcinoma exhibited the lowest risk (RR, 0.58; P=0.001). Differences in organ involvement and in histological type led to varying GI complications. It was also indicated that chemotherapy was associated with a decreased risk of hemorrhage (P=0.006), but there was no reduction in the risk of hemorrhage associated with perforation and obstruction (P>0.05). The median overall survival time of GMLC patients was 2.8 months (range, 0-108 months). The survival analyses revealed that perforation and extra-GI metastasis were negative prognostic factors but abdominal surgery was identified a positive prognostic factor. In conclusion, the histological distribution of GMLC differed from that of primary lung cancer. Sufficient and careful patient evaluation, targeted surgeries and systemic therapies for specific patients are able to increase patient survival rate and improve the quality of life.

Introduction

As a common cancer and the leading cause of cancer-associated mortality, lung cancer has always been universally associated with poor patient prognosis (1). The incidence and mortality rates of lung cancer occupy the first or second position in malignant tumors in China and the United States (2,3). Until 2015, the 5-year total survival rate for lung cancer was ≤20% in developed and developing countries (4). Between 40 and 50% of patients present with distant metastases upon diagnosis with lung cancer have a poor 5-year survival rate of <5% (1). Small cell lung cancer accounts for only 10% of lung cancer but non-small cell lung cancer accounts for ~90%, including squamous cell carcinoma, adenocarcinoma, large cell carcinoma, adenosquamous carcinoma and sarcomatoid carcinoma (4).

As demonstrated in autopsy studies, lung cancer metastases may be identified in every organ system (4). However, the gastrointestinal (GI) tract is not a common site of metastasis for primary lung cancer when compared with other sites, including bone, brain, liver and adrenal glands (5). Gastrointestinal metastases of lung cancer (GMLC) was caused by hematogenous spread and occurred at the end-stage of lung cancer. The incidence of GMLC was <2% in clinical studies, which was much lower compared with its prevalence identified during autopsies (5-8). In previous studies, GMLC was described primarily in case reports. Systemic survival analyses and association between clinicopathological factors, therapeutic factors and GI complications were seldom discussed. The present study reviewed >130 studies from the last 50 years and analyzed 366 cases of GMLC to reveal its clinical and prognostic characteristics by univariate and multivariate survival analyses.

Patients and methods

Patients. A total of 33 cases of GMLC from 32 Chinese articles (9-40) and 3 cases from the School of Medicine, Second
Affiliated Hospital of Zhejiang University (Hangzhou, China). The 3 cases were presented to the hospital between 2008 and 2015 and were collected in the present study. The Chinese literature was obtained from the VIP Journal Integration Platform (Chongqing, China; http://lib.cqvip.com/) published between 1993 and 2013. A total of 95 articles (5,8,41-133) from the PubMed database from 1961 to 2013 were reviewed, and 330 cases of GMLC were included. In all 366 cases of GMLC assessed, demographic and clinicopathological information was recorded and reviewed, including ethnicity, sex, age, pathology, initial lung cancer stage and therapy, interval between lung cancer diagnosis and identification of GMLC, clinical presentation, location, diameter and number of gross metastases, other metastatic site locations at the time of GMLC, GI surgeries, survival information and immunohistochemical information.

Disease classification. The histological classification of primary lung cancer was performed according to the 2004 World Health Organization classification system of lung tumors (134). The Tumor-Node-Metastasis staging was performed according to the 7th edition of the 2010 American Joint Committee on Cancer Staging manual (135). The histological distribution data of primary lung cancer was acquired from the International Lung Cancer Consortium (136).

Statistical analysis. \( \chi^2 \) test and Fisher's exact test were used to compare the incidence rates of different groups. Overall survival (OS) time was measured from the date of GMLC diagnosis to the date of mortality. This end point was computed using the Kaplan-Meier product limit method and the groups were compared using the log-rank test. Univariate and multivariate analyses of OS time were performed using Cox proportional hazards model. Only the variables with \( P<0.25 \) in the univariate analysis were included in the multivariate analysis model and, the backward sequencing method was used (137). The variables in the univariate and multivariate analyses included region (Asia vs. The Americas vs. Europe), histological type of lung cancer (squamous cell carcinoma vs. adenocarcinoma vs. large cell carcinoma vs. small cell lung cancer vs. adenosquamous carcinoma vs. sarcomatoid carcinoma), time (synchronous vs. metachronous), number (solitary vs. multiple), the organ where metastasis has been identified (esophagus vs. stomach vs. small intestine vs. colorectum vs. multiple organs), extra-GI metastasis (yes vs. no), perforation (yes vs. no), surgery of primary lung cancer (yes vs. no) and abdominal surgery (yes vs. no). Metastasis was considered synchronous if the interval of diagnosis between lung cancer and GI metastasis was <1 month. Metastasis was considered metachronous if the interval was >1 month. \( P<0.05 \) (two-sided) was considered statistically significant. The statistical analyses were performed using SPSS Statistics software (version 19.0; IBM Corp., Armonk, NY, USA).

Results

Patient and tumor characteristics. As presented in Table I, the majority of the patients were from Asia (62.3%) and >80% of them were male. The three countries with the greatest number of patients analyzed were Japan (139 cases), China (65 cases) and the United States (64 cases). The median age was 63 years (range, 31-92 years). The small intestine was the most frequently involved organ (59.6%) in the GI tract, and the colorectum ranked second (25.6%). Of the small intestine cases of GMLC, where the site of metastasis was specific, the majority of cases (63.4%) occurred in the jejunum. GI perforation (42.0%), hemorrhage (24.6%) and obstruction (20.4%) were the three most common complications. Synchronous and metachronous metastases were similarly probable (46.2% vs. 53.8%). The median time of metachronous patients from primary cancer diagnosis to GI metastasis was 6 months (range, 1-108 months). Solitary GMLCs were present in an increased number of patients compared with multiple metastases (69.4% vs. 30.6%). Furthermore, extra-GI metastases were present in the majority of patients (70.5%). The liver, brain, bone and adrenal gland were the four most prevalent sites of metastasis (data not shown), which was expected. In total, ~1/3 of the patients (33.3%) underwent surgical resection to remove the primary cancer and surgeries were performed in the GI tract in 75.8% of patients. Partial gastrectomy and enterectomy were the main types of abdominal resections performed (86.5%). These statistics are based solely upon cases where data was available.

Squamous cell carcinoma (28.5%), adenocarcinoma (27.6%) and large cell carcinoma (20.9%) were the three most common histological types of GMLC. When the histological distributions between GMLC and primary lung cancer were compared, it was observed that there was an increased frequency of GMLC of large cell carcinoma, small cell lung cancer and squamous cell carcinoma compared with GMLC of adenocarcinoma and other types of cancer (\( P<0.01 \); Table II).

Complications. The association between involved organs, histological type and GI complications is presented in Table III. Perforation of the small intestine (63.7%) occurred more frequently compared with perforation of stomach and colorectum (\( P<0.001 \)). The organs at risk of hemorrhage, from most to least common, were the stomach, colorectum and small intestine (\( P<0.05 \) in comparisons between two organs). No obstruction occurred in all 36 patients with gastric metastasis, and the incidence of obstruction was much lower compared with colorectum (\( P=0.003 \)) or small intestine (\( P=0.003 \)). In all the histological types of lung cancer analyzed, sarcomatoid carcinoma exhibited the lowest likelihood of perforation and the greatest likelihood of hemorrhage (\( P<0.05 \)). The risks of perforation of squamous cell carcinoma and small cell lung cancer were increased compared with the risks associated with adenocarcinoma (\( P<0.05 \)). The risks of hemorrhage of squamous cell carcinoma and small cell lung cancer were lower compared with the risks for large cell carcinoma (\( P<0.05 \)). No statistically significant difference was observed between two other organs or histological types (\( P>0.05 \)). No significant association was identified between histological type and GI obstruction (\( P>0.05 \)).

The association between GI complications and chemotherapy is indicated in Table IV. In total, ~1/4 (26.5%, 97/366) of the cases analyzed contained patient data of chemotherapy. Hemorrhage was more common in patients with GMLC who received no chemotherapy (\( P=0.006 \)). There was no significant
difference in the risks of perforation and obstruction between patients who had received and had not received chemo-

therapy (P>0.05).

Immunohistochemical analysis. In total, there were 35 cases

for which immunohistochemical data were available. Information from this limited number of cases illustrated that

a typical immunohistochemical staining of GMLC was posi-
tive for thyroid transcription factor -1 (TTF-1; 84.4%, 27/32)

and cytokeratin 7 (CK7, 96.6%, 28/29), but negative for CK20

(96.6%, 28/29) and caudal-related homeodomain transcrip-
tion 2 (CDX2, 100%, 23/23).

Survival estimates. Survival rate data was available for 268 of

the 366 patients studied. A total of 246 patients had succumbed

to disease by the end of the duration of the study, and the data of

the other 22 patients were censored data. The median OS time

was 2.8 months (range, 0-108 months, Fig. 1A). Univariate Cox

analysis (Table V) revealed that patients from the Americas

exhibited poorer prognoses compared with patients from

Asia (P<0.001). It was also indicated that the survival rates

for patients with small cell lung cancer and sarcomatoid carci-

noma were increased compared with patients with squamous

cell carcinoma (unadjusted hazard ratios (HRs), 0.62 (P=0.03)

and 0.34 (P=0.005), respectively). The other prognostic factors,

which indicate a poor survival outcome, included synchronous

metastasis, perforation of GMLC, extra-GI metastasis and

lack of abdominal surgery (P<0.05). Patients with multiple

metastases exhibited marginal poorer prognoses compared

with patients with solitary metastases (P=0.06). There were no

statistical significance between overall survival rate and other

factors, (sex, age, organs of GI metastasis, and surgery on the

primary lung cancer) (P>0.05).

In multivariate analysis, following adjustment for prog-

nostic factors, the region where the patients were from,

Table I. Continued.

C, Treatment factors

| Treatment                              | Patients, n | Percentage |
|----------------------------------------|-------------|------------|
| Lung cancer surgery                    |             |            |
| (not reported in 234 cases)            |             |            |
| No                                     | 88          | 66.7       |
| Yes                                    | 44          | 33.3       |
| Abdominal surgery                      |             |            |
| (not reported in 180 cases)            |             |            |
| No                                     | 45          | 24.2       |
| Yes                                    | 141         | 75.8       |

*Metastasis in the small intestine: Duodenum, 19 cases; jejunum, 104 cases; ileum, 41 cases; not otherwise specified, 60 cases. 
Metastasis in the colorectum: Appendix and ileocecus, 10 cases; colon, 78 cases; rectum, 5 cases. *Abdominal surgery: Partial gastrectomy and enterectomy, 122 cases; gastrointestinal fistula, bypass surgery and repair of the perforation, 7 cases; not otherwise specified, 12 cases.

Table I. Patient, tumor and treatment characteristics of 366 cases of gastrointestinal metastases of lung cancer.

A, Demographic factors

| Characteristics | Patients, n | Percentage |
|-----------------|-------------|------------|
| Region          |             |            |
| Asia            | 228         | 62.3       |
| America         | 67          | 18.3       |
| Europe          | 71          | 19.4       |
| Sex (not reported in 114 cases) |             |            |
| Male            | 208         | 82.5       |
| Female          | 44          | 17.5       |
| Age, years (not reported in 13 cases) |             |            |
| ≤54             | 54          | 15.3       |
| 55-64           | 133         | 37.7       |
| 65-74           | 116         | 32.9       |
| ≥75             | 50          | 14.2       |

B, Tumor factors

| Characteristics | Patients, n | Percentage |
|-----------------|-------------|------------|
| Involved organ (not reported in 10 cases) |             |            |
| Esophagus       | 1           | 0.3        |
| Stomach         | 40          | 11.2       |
| Small intestine$^a$ | 212         | 59.6       |
| Colorectum$^b$  | 91          | 25.6       |
| Multiple organs | 12          | 3.4        |
| Complications (not reported in 9 cases) |             |            |
| Perforation     | 150         | 42.0       |
| Hemorrhage      | 88          | 24.6       |
| Obstruction     | 73          | 20.4       |
| Histological type (not reported in 22 cases) |             |            |
| Small cell lung cancer | 46          | 13.4       |
| Squamous cell carcinoma | 98          | 28.5       |
| Adenocarcinoma  | 95          | 27.6       |
| Large cell carcinoma | 72          | 20.9       |
| Sarcomatoid carcinoma | 15          | 4.4        |
| Adenosquamous carcinoma | 5           | 1.5        |
| Other types     | 13          | 3.8        |
| Synchronous or metachronous metastasis (not reported in 208 cases) |             |            |
| Synchronous     | 73          | 46.2       |
| Metachronous    | 85          | 53.8       |
| Number of GI metastasis (not reported in 268 cases) |             |            |
| Solitary        | 68          | 69.4       |
| Multiple        | 30          | 30.6       |
| Extra-GI metastasis (not reported in 220 cases) |             |            |
| No              | 43          | 29.5       |
| Yes             | 103         | 70.5       |

difference in the risks of perforation and obstruction between patients who had received and had not received chemotheray (P>0.05).

Immunohistochemical analysis. In total, there were 35 cases for which immunohistochemical data were available. Information from this limited number of cases illustrated that a typical immunohistochemical staining of GMLC was positive for thyroid transcription factor-1 (TTF-1; 84.4%, 27/32) and cytokeratin 7 (CK7, 96.6%, 28/29), but negative for CK20 (96.6%, 28/29) and caudal-related homeodomain transcription 2 (CDX2, 100%, 23/23).

Survival estimates. Survival rate data was available for 268 of the 366 patients studied. A total of 246 patients had succumbed to disease by the end of the duration of the study, and the data of the other 22 patients were censored data. The median OS time was 2.8 months (range, 0-108 months, Fig. 1A). Univariate Cox analysis (Table V) revealed that patients from the Americas exhibited poorer prognoses compared with patients from Asia (P<0.001). It was also indicated that the survival rates for patients with small cell lung cancer and sarcomatoid carcinoma were increased compared with patients with squamous cell carcinoma (unadjusted hazard ratios (HRs), 0.62 (P=0.03) and 0.34 (P=0.005), respectively). The other prognostic factors, which indicate a poor survival outcome, included synchronous metastasis, perforation of GMLC, extra-GI metastasis and lack of abdominal surgery (P<0.05). Patients with multiple metastases exhibited marginal poorer prognoses compared with patients with solitary metastases (P=0.06). There were no statistical significance between overall survival rate and other factors, (sex, age, organs of GI metastasis, and surgery on the primary lung cancer) (P>0.05).

In multivariate analysis, following adjustment for prognostic factors, the region where the patients were from,
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Discussion

As the digestive tract remains a rare site of metastasis of primary lung cancer, GMLC was previously described primarily in case reports (8). The clinical incidence of GMLC was <2% in patients with primary lung cancer and >10% in autopsy-associated studies (5-8). The majority of GMLC cases occurred at the end-stage of lung cancer, and misdiagnosis and missed diagnosis occurred frequently (138). In the present study, the sex and age of the patients with GMLC was similar with cases reported in previous studies with small sample sizes (7,8). In the present study, the majority of the patients were elderly men.

The intestines, particularly the small intestine, were the main organs involved in GMLC, owing to their abundant blood supply. There were certain patients that presented with metastases in multiple GI organs, due to the lethality of the first involved organ and the involvement of additional GI organs. On account of the significant difference between the GMLC incidences from clinical and autopsy-associated studies, the majority of the patients with GMLC were subclinical with minimal or no symptoms. The symptoms of GMLC always appeared alongside clinical complications, including GI perforation, hemorrhage and obstruction. The incidence of severe histological type, GI perforation, extra-GI metastasis and abdominal surgery remained prognostic factors for survival rate. Other factors were not significant (Table V; Fig. 1B-D).
The diagnosis of GMLC is not easy owing to its non-specific symptoms, although its complications are well known. When patients with lung cancer complain of potential GMLC symptoms (abdominal pain, nausea, vomiting, anemia, hematochezia, melema, constipation or other changes in bowel habits), particularly those that cannot be explained by primary lung cancer or undergoing chemotherapy or radiotherapy treatment, GMLC should be considered. As part of systemic metastases, GMLC is caused by hematogenous dissemination (8). In previous studies (88,141), 42.9-100.0% of the patients with GMLC had extra-GI metastasis, and this ratio was 70.5% in the present study. Therefore, it is necessary for patients with GMLC to undergo sufficient evaluations prior to initiation of treatment (142). On the other hand, it was reported that GMLC was more common in patients with metastases in adrenal glands, kidneys and celiac lymph nodes compared with patients with other type of metastases (5). However, this finding was not supported by the data in the present study.

Laboratory examination, endoscopy, gastroenterography, computed tomography (CT) and positron-emission tomography (PET)-CT may aid the diagnosis of GMLC (120). In a study by Kim et al (141) on the signs of GMLC in CT, it was reported that positive signs could be identified in 93% of patients, including localized GI wall thickening, the presence of a mass in the GI cavity, regional glandular enlargement, indigitation and perforation. PET-CT was able to assist the detection of subclinical GMLC and systemic evaluation of extra-GI metastases (133,143,144). Pathology was a critical factor in diagnosis. The pathology of primary lung cancer should be reviewed and compared with that of GMLC. In the present study, in the majority of cases of GMLC considered, there was positive immunohistochemical staining for thyroid transcription factor 1 and cytokeratin-7 but negative staining for CK20 and CDX2, which was consistent with a previous study (8).

As the end-stage of lung cancer, GMLC was always associated with a poor prognosis (69). In the present study, the median OS time was 2.8 months and 53.4% of the patients succumbed to disease within 3 months of diagnosis of GMLC. Only 9.0% (24/268) of patients were reported to survive for >1 year and 2 patients (0.7%) with large cell carcinoma survived >7 years. Patients in the dataset analyzed by the present study generally exhibited longer overall survival times compared with patients assessed by Garwood et al (69). The patients that Garwood et al (69) studied are part of the present dataset. All patients in the study by Garwood et al (69) exhibited perforation of the small intestine, which appears to be associated with shorter OS (based on comparisons between the results of the present study and Garwood et al (69). In the present study, there were five factors, including region, histological type, GI perforation, extra-GI metastasis and surgical resection, which formed the final components included in the multivariate Cox
Table V. Univariate and multivariate Cox regression analyses of variables that may affect overall survival of patients with gastrointestinal metastases of lung cancer.

A, Univariate analysis

| Variable                              | Overall survival |
|---------------------------------------|------------------|
|                                       | HR   | 95% CI   | P-value |
| Demographic factors                   |      |         |        |
| Region                                |      |         |        |
| Asia                                  | 1.00 |         |        |
| America                               | 3.27 | 2.32-4.59 | <0.001 |
| Europe                                | 1.27 | 0.92-1.76 | 0.148  |
| Sex                                   |      |         |        |
| Male                                  | 1.00 |         |        |
| Female                                | 0.81 | 0.53-1.25 | 0.351  |
| Age, years                            |      |         |        |
| ≤54                                   | 1.00 |         |        |
| 55-64                                 | 0.86 | 0.60-1.25 | 0.430  |
| 65-74                                 | 0.96 | 0.66-1.42 | 0.849  |
| ≥75                                   | 1.27 | 0.78-2.07 | 0.339  |
| Histological type                     |      |         |        |
| Squamous cell carcinoma               | 1.00 |         |        |
| Adenocarcinoma                        | 0.78 | 0.55-1.10 | 0.150  |
| Large cell carcinoma                  | 0.75 | 0.52-1.08 | 0.123  |
| Small cell lung cancer                | 0.62 | 0.41-0.96 | 0.031  |
| Adenosquamous carcinoma               | 2.01 | 0.73-5.56 | 0.177  |
| Sarcomatoid carcinoma                 | 0.34 | 0.16-0.72 | 0.005  |
| Time of GI metastasis                 |      |         |        |
| Synchronous                           | 1.00 |         |        |
| Metachronous                          | 0.62 | 0.43-0.90 | 0.011  |
| Number of GI metastasis               |      |         |        |
| Solitary                              | 1.00 |         |        |
| Multiple                              | 1.64 | 0.98-2.76 | 0.064  |
| GI metastasis organ                   |      |         |        |
| Esophagus’                            | N/A  |         |        |
| Stomach                               | 1.00 |         |        |
| Small intestine                       | 1.19 | 0.82-1.73 | 0.367  |
| Colorectal                            | 0.78 | 0.48-1.28 | 0.321  |
| Multiple organs                       | 0.95 | 0.44-2.05 | 0.886  |
| Perforation                           |      |         |        |
| No                                    | 1.00 |         |        |
| Yes                                   | 2.13 | 1.61-2.78 | <0.001 |
| Extra-GI metastasis                   |      |         |        |
| No                                    | 1.00 |         |        |
| Yes                                   | 2.94 | 1.85-4.76 | <0.001 |
| Treatment factors                     |      |         |        |
| Surgical resection of the primary cancer |    |         |        |
| No                                    | 1.00 |         |        |
| Yes                                   | 0.68 | 0.43-1.04 | 0.078  |
| Abdominal surgery                     |      |         |        |
| No                                    | 1.00 |         |        |
| Yes                                   | 0.53 | 0.35-0.78 | 0.001  |
Table V. Continued.

B, Multivariate analysis

| Variable                        | Overall survival |       |       |
|---------------------------------|------------------|-------|-------|
|                                 | Adjusted HR      | 95% CI| P-value |
| Demographic factors             |                  |       |       |
| Region                          |                  |       |       |
| Asia                            | 1.00             |       |       |
| America                         | 3.91             | 2.41-6.34 | <0.001 |
| Tumor factors                   |                  |       |       |
| Histological type               |                  |       |       |
| Squamous cell carcinoma         | 1.00             |       |       |
| Adenosquamous carcinoma         | 5.57             | 1.84-16.83 | 0.002  |
| Perforation                      |                  |       |       |
| No                              | 1.00             |       |       |
| Yes                             | 2.00             | 1.26-3.17 | 0.003  |
| Extra-GI metastasis             |                  |       |       |
| No                              | 1.00             |       |       |
| Yes                             | 1.92             | 1.12-3.29 | 0.018  |
| Treatment factors               |                  |       |       |
| Surgical resection              |                  |       |       |
| No                              | 1.00             |       |       |
| Yes                             | 0.47             | 0.28-0.81 | 0.006  |
| Other factors                   |                  |       |       |
|                                 |                  |       |       |

*Esophageal metastasis in 1 case. HR, hazard ratio; CI, confidence interval; GI, gastrointestinal; NS, not significant.

Figure 1. (A) OS of patients with gastrointestinal metastases of lung cancer. Variables affecting OS in multivariate Cox regression analysis: (B) Perforation, (C) extra-GI metastasis and (D) abdominal surgery. GI, gastrointestinal; HR, hazard ratio; OS, overall survival.
model. Although it was indicated that the survival times for Asian patients were longer compared with American patients, region was not a useful factor in determining survival times as American studies assessed in the present study were undertaken on average ~20 years earlier compared with the studies from Asia. With an adjusted hazard ratio of 5.57 (P=0.002), it was indicated that patients with adenosquamous carcinoma had a significantly poorer prognosis compared with patients with squamous cell carcinoma based on multivariate Cox analysis. However, only four cases of adenosquamous carcinoma were available in the present survival analysis, so this result is of limited value. Perforation of GMLC and extra-GI metastasis were indicated to be negative prognostic factors, but abdominal surgery appeared to be a positive prognostic factor. However, the selective bias of the patients, particularly in treatment choice, must be considered in the present retrospective study. The patients with less severe general conditions were more likely to undergo surgery than those in critical conditions.

The present study revealed that, due to the increasing incidence of lung cancer, as well as the ability of modern medicine to prolong the life of lung cancer patients, GMLC is no longer rare. On the basis of the assessment performed in the present study, the histological distribution of GMLC was different from that of primary lung cancer. Early detection, diagnosis and treatment are central to improving patient prognosis. Sufficient and careful evaluations, targeted surgeries and systemic therapies for specific patients following discussion between multi-disciplinary teams of medics are able to improve the survival rate and quality of life of patients (138,145). The main purpose of surgery is to relieve symptoms while causing the least trauma possible to the patient. Data from the present study revealed that >30% of the patients had multiple metastases in their GI tract, therefore careful investigations during the surgery are required to avoid subclinical metastases being missed.

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