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ORIGINAL ARTICLE

One Case of Metachronous Dual Primary Tumors

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Abstract

This study is to explore the respects of a rare case of metachronous dual primary tumors like clinical characteristics, diagnostic methods, surgical treatment and chemotherapy strategies. The patient's first primary tumor was duodenal ampullary carcinoma at age 65, while the colon cancer was diagnosed 39 months later as the second primary tumor. The patient received treatments as pancreaticoduodenectomy, GS chemotherapy, and right hemicolectomy as well as XELOX chemotherapy. Follow-up of duodenal ampullary carcinoma has been 3 years and colon cancer has been 1 year after surgery. No sign of recurrence or metastasis has been found. The results of this study show that it is feasible to adopt an individualized comprehensive treatment strategy for patients with Metachronous Double Primary Tumors, which can offer a reference for similar cases.

Keywords: **Primary duodenal ampulla cancer; Colon Cancer; Multiple Primary tumors; Metachronous; Treatment;**

Introduction

With the improvement of diagnosis and treatment of malignant tumors combined with the extension of patients' survival, the incidence of multiple primary malignancies (MPM) has increased in singulos annos, seriously affecting patients' survival and living quality[1]. MPM refers that two or more primary malignant tumors in the same host occur synchronously or metachronously in a single or multiple organs or tissues[2]. Depending on the number of organs in which the tumors occur, they can be called biprimary, triprimary , or quadruple primary tumors, etc. [2]The article reports a case of a patient with metachronous dual primary tumors that the first primary tumor was duodenal ampullary carcinoma and the second was colon cancer.

Duodenal cancer, with low incidence and clinically rare, is a malignant tumor originating from the duodenal mucosal epithelium[3]. On the contrary, colon cancer is a common digestive system malignancy. The CUHK research team collected data from databases such as the Global Cancer Observatory , Cancer Incidence in Five Continents , and the Global Burden of Disease to calculate and analyze cancer incidence and the prevalence of various risk factors, founding that the disease burden caused by small intestinal cancer varies in different regions, with the highest incidence in developed regions such as North America, Oceania, and Northern Europe[4, 5]. In the past 10 years, the annual incidence of small intestinal cancer in North America was approximately 1.4 /100,000, of which duodenal cancer accounted for 60% to 70%, and the rest were jejunal and ileal cancers[6]. In the same year, the annual incidence of colorectal cancer was approximately 25.04/100,000[7]. This study aims to explore the clinical characteristics, diagnostic methods, surgical treatment, and chemotherapy strategies of a rare case of metachronous dual

primary tumors to offer a reference for clinical workers.

Clinical Data

The patient is a 65-year-old male with a height of 170 cm and a weight of 70 kg, who was previously healthy and denied any history of chronic diseases such as hypertension and diabetes, as well as any family history of cancer.

December 20, 2020, he was admitted to the 940th Hospital of Joint Logistics Support Force of Chinese People's Liberation Army (hereinafter referred to as "the hospital") due to "upper abdominal distension and pain for one month, and yellow skin and sclera for two weeks". He had upper abdominal distension and pain without obvious cause one month before admission, and yellow skin and sclera two weeks ago, itching all over the body, accompanied by nausea and vomiting. His abdominal MR examination in an external hospital showed: 1. Abnormal signal mass around the ampulla, low-lying bile duct obstruction, bile duct dilatation, and multiple retroperitoneal lymph nodes. Enhancement is recommended. His general condition has been good since the onset of the disease, with poor sleep and diet, strong tea-like urine, black stools, and a weight loss of 5kg in the past month. Laboratory tests after admission: hemoglobin 85g/L, fibrinogen 5.58g/L, total bilirubin 230.50umol/L, direct bilirubin 200.80umol/L, indirect bilirubin 29.70umol/L; fecal occult blood test positive; tumor indicators: carbohydrate antigen-199 >12000.0U/mL, carcinoembryonic antigen 6.81ng/mL. Abdominal CT suggests (Fig. 1): 1. Dilatation of intrahepatic and extrahepatic bile ducts, dilatation of pancreatic ducts, truncation of the lower segment of the common bile duct at the duodenal ampulla, and soft tissue shadows, which are often considered periampullary carcinoma. 2. Multiple enlarged lymph nodes are seen in the retroperitoneum, which are considered to be metastatic tumors. Electronic gastroscopy suggests (Fig. 2): duodenal papillary carcinoma, descending segment of the duodenum: the papilla can be seen with a half-circumferential cauliflower-like protrusion, with oozing blood, and the biopsy is brittle (see Figure 3 for biopsy results), which is easy to bleed. Electronic colonoscopy did not show obvious abnormalities.

With jaundice, total bilirubin 230.50umol/L, direct bilirubin 200.80umol/L, weight loss of 5kg before admission and malnutrition, he accepted PTCD external drainage treatment and enteral nutrition support. After PTCD drainage and enteral nutrition support for 2 weeks, hemoglobin was 103g/L, total bilirubin 71.50umol/L, and direct bilirubin 63.30umol/L, showing that the bilirubin decreased significantly and the nutritional status improved. On January 5, 2021, radical pancreaticoduodenectomy was performed under general anesthesia. Postoperative pathology showed (Fig. 4): moderately to poorly differentiated adenocarcinoma in the ampulla of the duodenum, and cancerous tissue metastasis found in the lymph nodes (4/11). After surgery, GS (gemcitabine+S-1) chemotherapy was given for 6 cycles. After the end of chemotherapy, imaging evaluation was performed regularly with no tumor recurrence or metastasis.

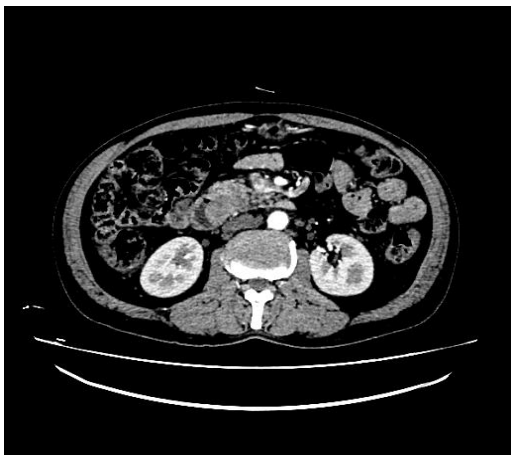

Figure 1: CT showed that the lower segment of

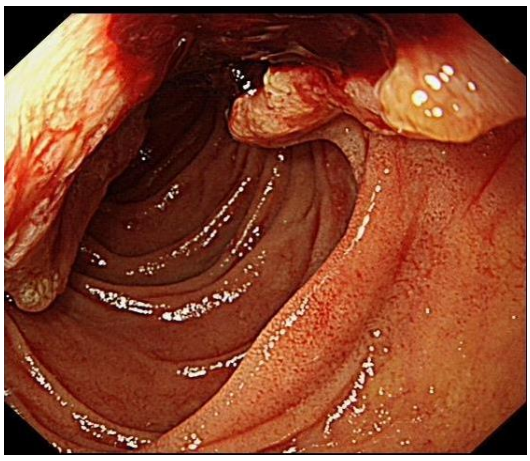

Figure 2: Electronic gastroscopy showed

the common bile duct was cut off at the ampulla of the duodenum, showing a cup-shaped change and soft tissue shadows, which was mostly considered to be periampullary cancer.

duodenal papillary carcinoma, and half of the duodenal papilla was seen to have a circumferential cauliflower-like protrusion.

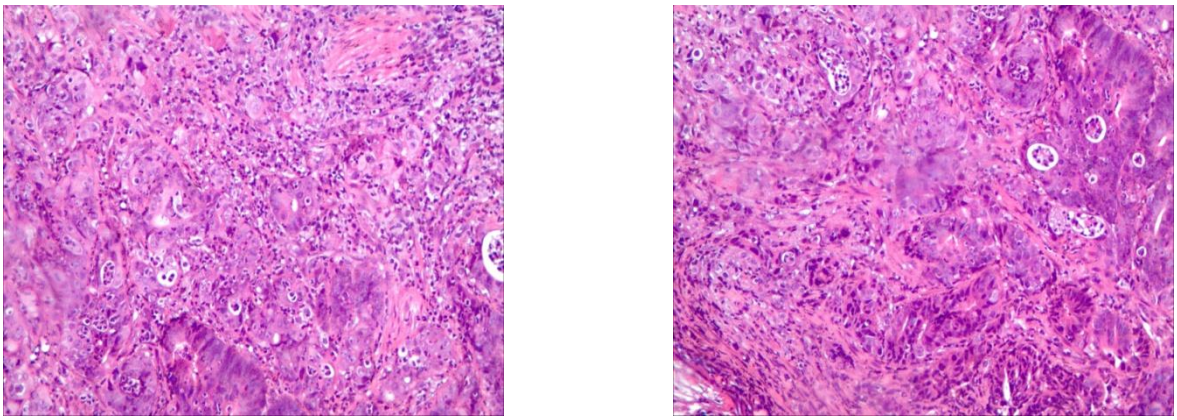

Figure 3: Duodenal pathological biopsy results: Immunohistochemistry: CKp (+), Villin (+), Syn (-), CgA (-), Ki67index≈80%, CDX2 (+). Pathological diagnosis: (duodenal) moderately to poorly differentiated adenocarcinoma .

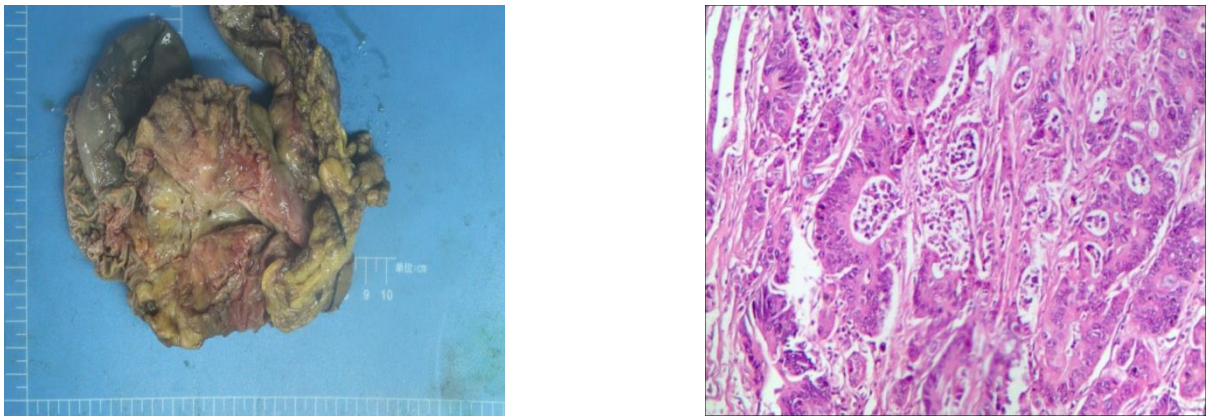

Figure 4: Postoperative duodenum pathological results: Immunohistochemistry: CK7 (-), CK20 part (+), Villin (+), CD34 blood vessels (+), CEA (+), CK8/18 (+), Pgp (-), GSTπ (+), TOP-II part (+), TS (-), TP53 (+), CDX2 part (+). Pathological diagnosis: moderately to poorly differentiated adenocarcinoma was in the duodenal ampulla. Cancer tissue invaded the entire layer of the duct wall, and some areas reached the periphery of the pancreas. No cancer tissue was found in the upper and lower resection margins, duodenal stump, common bile duct, and pancreatic tissue. Cancer tissue metastasis was found in lymph nodes (4/11).

On March 29, 2023, the patient was admitted to the hospital again because "more than 39 months after the operation of ampullary cancer, the tumor index was found to be elevated for 1 day". Tumor index at admission showed carcinoembryonic antigen was 6.16ng/mL and Abdominal ultrasound and CT was no obvious abnormalities. Electronic colonoscopy prompts (Fig. 5): There are multiple polyps in the colon. Ascending colon had cancer that huge ginger-like tumors can be seen protruding from the lumen of it with congestion and ulceration on the surface, a lot of necrotic tissue, attached feces, easy to bleed when touched, semi-circumferential, narrow intestinal cavity, 5 biopsies, and brittle texture. Hepatic flexure: 3 mucosal bulges of about 0.2-0.4cm in size can be seen with a smooth surface and normal color.

On April 7, 2023, the patient underwent "radical colon cancer resection+partial liver resection" under general anesthesia. Postoperative pathology showed (Fig. 6): moderately differentiated tubular

adenocarcinoma in ileocecal and ascending colon, with cancer tissue invading the serosa and liver invading the nerve bundles. Lymph node metastasis was detected (6/11). The patient received 6 cycles of chemotherapy with the XELOX regimen----capecitabine+oxaliplatin. Whereas, because of oxaliplatin allergy, the patient was switched to the "albumin paclitaxel+oxaliplatin+tegafur, gimeracil and oteracil potassium" chemotherapy regimen for 2 cycles. After the end of chemotherapy, imaging and pathological evaluations were performed regularly suggesting that no tumor recurrence or metastasis was found (Fig. 7).

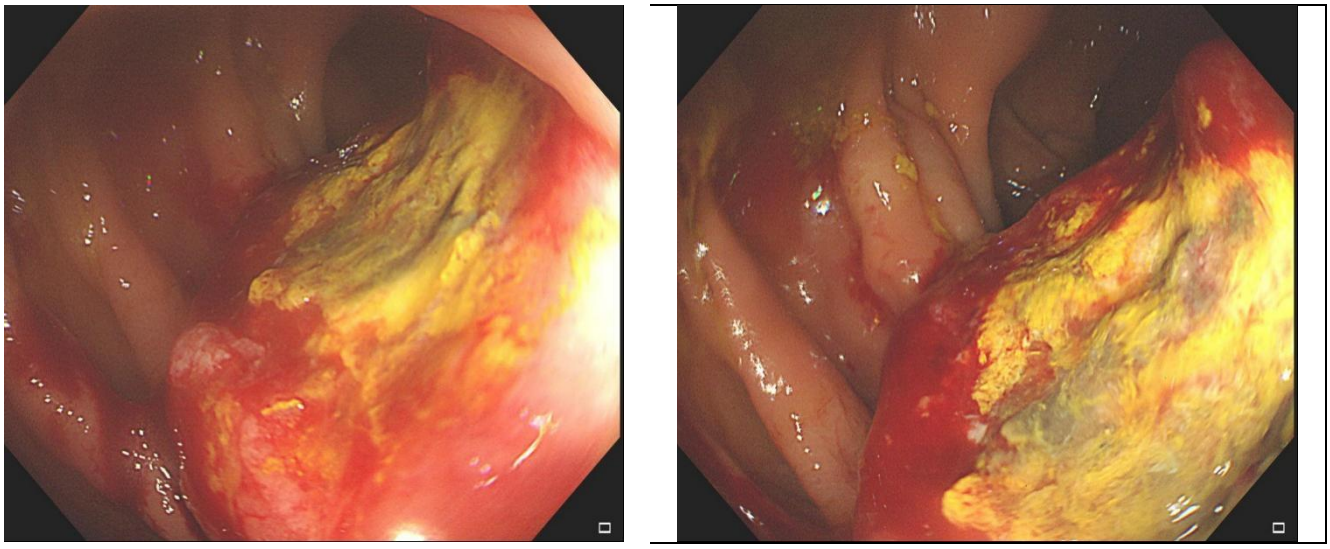

Figure 5: Electronic colonoscopy findings: A huge ginger-like mass can be seen protruding from the lumen of the ascending colon, with congestion and ulceration on the surface, lots of necrotic tissue, feces attached, easy to bleed when touched, semi-circumferential, and narrow intestinal lumen. Diagnosis: ascending colon cancer.

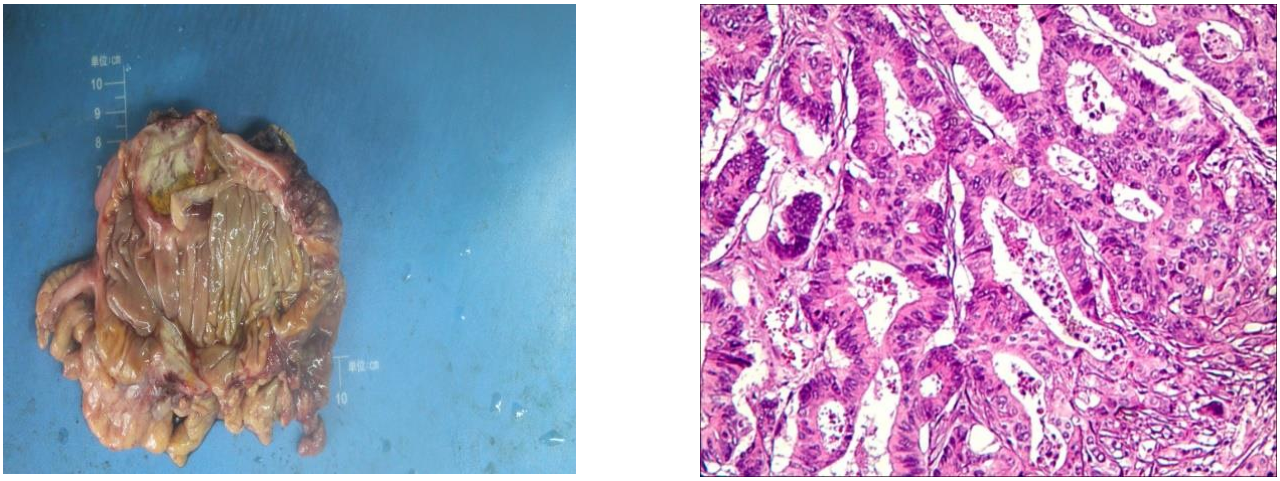

Figure 6: Postoperative pathological results of colon cancer: Immunohistochemistry: CKp (+), CK20 (partially +), CDX2 (partially +), TP53 (+), Ki67 (index≈40%), MLH1 (+), MSH2 (+), MSH6 (+), and PMS2 (+). Pathological diagnosis: ileocecal and ascending colon has moderately differentiated tubular adenocarcinoma, cancer tissue penetrates the serosa, involves the liver and invades the nerve bundle. No cancer tissue was found at the upper and lower resection margins, whereas, cancer metastasis was found in the lymph nodes (6/11).

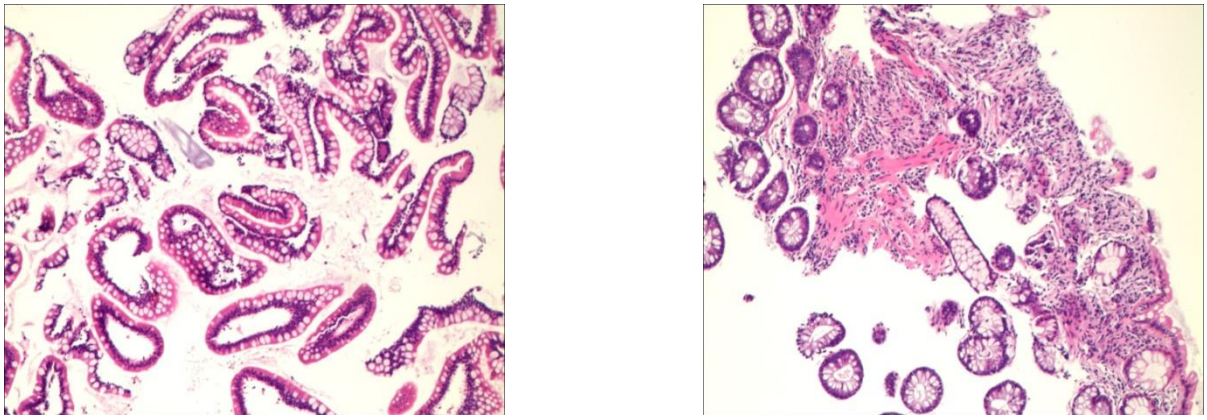

Figure 7: Anastomosis after colon malignant tumor surgery, rectal pathological biopsy results: mucosal gland hyperplasia, tight arrangement, and inflammatory cell infiltration. Pathological diagnosis: 1. Chronic inflammation of (anastomotic) mucosal tissue. 2. (Rectal) hyperplastic polyps.

Discussion

The overall incidence of MPM has a wide range from 2.4% to 17%[8, 9]. The fact that significant differences in the incidence reported by different countries may be related to such factors as study population, diagnostic criteria, and follow-up time[10]. With the continuous improvement of tumor diagnosis and treatment, clinicians have an improving cognition and recognition on MPM, and more detailed follow-up are contributed to the increasing detection rate of MPM. The exact cause of MPM is not clear, probably related to genes and genetic susceptibility factors. Though, special MPM hereditary tumor syndromes are confirmedly related to genetic defects[2].

This study reports one case of a male patient with metachronous dual primary tumors that his first and second primary tumors were duodenal ampullary carcinoma and colon cancer, respectively. The first primary tumor was diagnosed at his 65, and the two primary tumors has 39-month intervals. As is known to all, duodenal cancer, accounting for 60% to 70% of small intestinal cancers, is a rare malignant tumor[6]. Its diagnosis usually requires imaging examinations, endoscopy, and detection of serum tumor marker levels. On the other hand, colon cancer is a common malignant tumor of the digestive system. In terms of treatment, surgery is the main treatment for duodenal cancer and colon cancer, while chemotherapy and radiotherapy are used for preoperative and postoperative adjuvant treatments. Our case was treated with pancreaticoduodenectomy combined with GS chemotherapy for 6 cycles and right hemicolectomy combined with XELOX chemotherapy for colon cancer. The patients were followed up for 3 years after pancreaticoduodenectomy and 1 year after colon cancer surgery, suggesting that no sign of tumor recurrence or metastasis.

The reason why the prognosis was relatively good under the satiation that the cased patient suffered from both duodenal cancer and colon cancer is because both were discovered at an early stage. Nevertheless, the prognosis assessment of metachronous malignant tumors needs to consider comprehensively multiple factors, including tumor location, histological type, stage, patients' age, physical condition, and treatment plan. 1. Tumor location: The prognosis of duodenal cancer and colon cancer is quite different. The early symptoms of duodenal cancer are ambiguous which is easy to metastasize, and the prognosis is relatively poor, and vice versa. 2. Histological type: The histological types of duodenal cancer and colon cancer are diverse, and the prognosis of different types varies greatly. For example, duodenal adenocarcinoma has a poor prognosis, while duodenal neuroendocrine tumors have a relatively good prognosis. In colon cancer, invasive ductal carcinoma has a poor prognosis, while mucinous adenocarcinoma has a relatively good prognosis. 3. Tumor staging: Tumor staging is an important indicator for assessing prognosis. Early tumors have a good prognosis and vice versa. In this case, since both duodenal cancer and colon cancer were discovered at an early stage, the prognosis is relatively good. 4. Age and physical conditions: Patient who is older and in poor physical condition has a relatively poor

prognosis. 5. Treatment plan: A reasonable treatment plan is the key to improving prognosis. For early tumors, surgical resection is the preferred treatment method. For advanced tumors, it is necessary to choose a comprehensive treatment plan such as chemotherapy, radiotherapy, and targeted therapy according to the specific situation. 6. The mutual influence of metachronous tumors: The occurrence of metachronous tumors may affect each other, for example, the occurrence of colon cancer may increase the risk of duodenal cancer, and vice versa. Therefore, when evaluating the prognosis, the mutual influence between the two tumors needs to be considered.

Conclusion

In short, the diagnosis, treatment and prognosis assessment of metachronous multiple malignant tumors are a complex process required comprehensive consideration of multiple factors. Doctors need to develop a reasonable treatment plan based on the patient's specific situation and closely monitor the condition to improve survival rate and quality of life.

Funding

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Data Availability Statements

The data generated in the present study may be requested from the corresponding author.(E-mail:qinjianwei940@163.com)

The data generated in the present study are included in the figures and/or tables of this article.

Authors' Contributions

SYH and LYS analyzed the data and were the primary author of the manuscript. XSL acquired the CT scan images. LHX analyzed patient data. MBW and PYP confirm the authenticity of the data. QJW assisted in writing the manuscript. All authors have read and approved the final manuscript.

Patient Consent for Publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Competing Interests

The authors declare that they have no competing interests.

References

1. Mehmet; Sitki; Copur; Suresh; Manapuram, Multiple Primary Tumors Over a Lifetime. *Oncology* **2019,** *33* (7).
2. Vogt, A.; Schmid, S.; Heinimann, K.; Frick, H.; Herrmann, C.; Cerny, T.; Omlin, A., Multiple primary tumours: challenges and approaches, a review. *ESMO Open* **2017,** *2* (2).
3. PAN Jun, Q. S., YANG Ningrong, WANG Lin., Cox regression analysis of prognosis and clinical observation of first□line chemotherapy in advanced duodenal cancer. **2018,** *23* (1), 44-51.
4. Siegel, R. L.; Miller, K. D.; Wagle, N. S.; Jemal, A., Cancer statistics, 2023. *CA: a cancer journal for clinicians* **2023,** *73* (1), 17-48.
5. Jinsong, W.; Jiayan, W.; Min, P., Interpretation and enlightenment of 2023 American cancer statistics report and the latest global cancer statistics. **2023,** *38* (6), 523-527.
6. Suradkar, K.; Lebwohl, B.; Green, P.; Neugut, A.; Kiran, R. P., Incidence and Survival for Small Bowel Tumors over the Last Two Decades (1991-2012): A SEER-based Analysis. *Journal of the American College of Surgeons* **2016,** *223* (4, Supplement 2), e106.
7. Legué, L. M.; Bernards, N.; Gerritse, S. L.; van Oudheusden, T. R.; de Hingh, I. H.; Creemers, G. M.; Ten Tije, A. J.; Lemmens, V. E., Trends in incidence, treatment and survival of small bowel adenocarcinomas between 1999 and 2013: a population-based study in The Netherlands. *Acta oncologica (Stockholm, Sweden)* **2016,** *55* (9-10), 1183-1189.
8. Weir, H. K.; Johnson, C. J.; Thompson, T. D., The effect of multiple primary rules on population-based cancer survival. *Cancer Causes Control* **2013,** *24* (6), 1231-42.
9. Coyte, A.; Morrison, D. S.; McLoone, P., Second primary cancer risk - the impact of applying different definitions of multiple primaries: results from a retrospective population-based cancer registry study. *BMC cancer* **2014,** *14*, 272.

10. Wood, M. E.; Vogel, V.; Ng, A.; Foxhall, L.; Goodwin, P.; Travis, L. B., Second malignant neoplasms: assessment and strategies for risk reduction. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology* **2012,** *30* (30), 3734-45.