

Current status of surgical treatment of rectal cancer in China

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Abstract

With the changing lifestyle and the acceleration of aging in the Chinese population, the incidence and mortality of colorectal cancer (CRC) have risen in the last decades. On the contrary, the incidence and mortality of CRC have continued to decline in the USA since the 1980s, which is mainly attributed to early screening and standardized diagnosis and treatment. Rectal cancer accounts for the largest proportion of CRC in China, and its treatment regimens are complex. At present, surgical treatment is still the most important treatment for rectal cancer. Since the first Chinese guideline for diagnosis and treatment of CRC was issued in 2010, the fourth version has been revised in 2020. These guidelines have greatly promoted the standardization and internationalization of CRC diagnosis and treatment in China. And with the development of comprehensive treatment methods such as neoadjuvant chemoradiotherapy, targeted therapy, and immunotherapy, the post-operative quality of life and prognosis of patients with rectal cancer have improved. We believe that the inflection point of the rising incidence and mortality of rectal cancer will appear in the near future in China. This article reviewed the current status and research progress on surgical therapy of rectal cancer in China.

Keywords: Rectal cancer; Incidence trend; Early screening; Surgical treatment

Introduction

According to the GLOBOCAN 2018 assessment of cancer incidence and mortality published by the International Agency for Research on Cancer, there were over 1.8 million new colorectal cancer (CRC) cases and 881,000 deaths in 2018.^[1] CRC accounted for approximately one out of every ten cancer cases and deaths. Overall, CRC ranks third in terms of cancer incidence and second in terms of cancer-related mortality. The highest incidence rates of colon cancer are found in parts of Europe, Australia/New Zealand, North America, and Eastern Asia (Japan, Korea, and Singapore [in females]), with Hungary ranking first among males and Norway ranking first among females. The incidence rate of rectal cancer has a similar geographical distribution and the highest incidence rates are found in Korea (male) and Macedonia (female).^[1] In China, the standardized incidence of CRC in 2018 was 23.7/100,000, placing it second in China and fifty-fourth in the world. The standardized mortality was 10.9/100,000, ranking fifth in China and forty-third in the world. However, due to the large population base, China accounted for 28.2% of the total number of cases and 28.1% of the total number of

deaths worldwide, ranking first in the world.^[2,3] In recent years, with the changing lifestyle and the acceleration of aging the incidence and mortality of CRC have risen in China, which endangers the health of residents and places a heavy burden on the economy.^[4,5]

Incidence Trend and Overall Survival (OS)

The incidence and mortality of CRC vary greatly among different countries due to disparities in socio-economic development and lifestyle. Arnold *et al*^[6] reported that countries with increased incidence and mortality in the last decade include Russia, China, and Brazil, while the USA, Japan, and France all decreased. According to statistics released in 2020, the incidence and mortality of CRC in the USA have declined rapidly since 2000.^[7] The incidence of CRC in the USA decreased by an average annual rate of 2.5% from 2007 to 2016, and mortality decreased by 2.1% annually from 2008 to 2017.^[7] In contrast, according to the China Cancer Center the incidence of CRC in China increased by an average rate of 4.2% annually from 2000 to

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2005 and by 1.3% annually from 2006 to 2011, while mortality increased by 1.6% annually between 2000 and 2011.^[4,5]

In recent years, although the overall incidence of CRC in the USA has remained on the decline, it has increased in younger people under 50 years of age, and the largest increase has been in rectal cancer, followed by distal colon cancer.^[7,8] The majority of CRC in Asia, is rectal cancer, accounting for more than 50% of all cases, compared to Europe and North America, where rectal cancer accounts for less than 40% of all CRC cases.^[9] In China, an increase in the proportion of proximal colon tumors (the “right shift” of the tumor site) has been observed since 1980.^[10-12] The proportion of rectal cancer cases decreased significantly from 71.2% in the 1980s to 66.7% in the 1990s, but the proportion of ascending and transverse colon cancer continued to increase, from 10.9% in the 1980s to 15.2% in the 1990s.^[13] At present, the reason (s) for these changes are not clear, but may be related to factors such as improved diagnostic methods and different etiologies of CRC.

The stage at diagnosis is the most important predictor of survival. In the USA, the 5-year OS for CRC ranges from 90% for patients diagnosed with localized disease to 14% for those diagnosed with distant metastases disease.^[7] The 5-year OS in China is lower than that in the USA (2012–2015: 56.9% vs. 2009–2015: 64%).^[7,14] The 5-year OS is higher in Chinese cities (59.3%) than in rural areas (52.6%).^[14] According to the tumor-node-metastasis staging system, the 5-year OS for rectal cancer is slightly lower than that for colon cancer (stage I: 88%; stage IIA: 81%; stage IIB: 50%; stage IIIA: 83%; stage IIIB: 72%; stage IIIC: 58%; and stage IV: 13%).^[15] Due to the imbalance of social and economic development in China, the level of medical services varies greatly between regions; therefore, the diagnosis and treatment of CRC also vary widely by region. Gu *et al*^[16] analyzed the survival of 1321 patients treated in the Peking University Cancer Hospital from 1999 to 2009 and reported that the 5-year OS of CRC patients was 62.6% (rectal cancer: 63.2%). This was significantly higher than the national average of 47.2% in China. It was also higher than the 5-year OS reported in Europe (56.8%) but lower than that of the USA (64.7%).

Early Screening and Clinical Staging

Early screening is undoubtedly an important method to reduce the incidence and mortality of CRC. As early as 2016, 68% of adults aged 50 to 75 years in the USA received CRC screening.^[17] Thus far, CRC screening has been carried out in some developed cities in China such as Tianjin, Shanghai, Hangzhou, and Guangzhou, but is not yet conducted nationwide. In 2017, Gu *et al* performed a meta-analysis on population compliance with CRC screening in China from 2006 to 2015.^[18] A total of 827,904 people were enrolled for colonoscopy screening. The final rate of participant compliance was determined to be only 44%. Early-stage diagnosis of CRC in China is less than 10%,^[19] markedly lower than in Japan and Korea. Early CRC diagnosis in Japan had reached 20% by 1991, while in South Korea it had exceeded 20% by 2009.^[20,21] There are numerous potential reasons for the low rate of

early detection in China, among them uneven development in various cities, poor overall compliance, and negative reactions to endoscopy.^[19] Data published by the National Cancer Center of China in 2019 reported that 1,381,561 qualified participants from 16 provinces in China were recruited for a risk-score assessment combined with colonoscopy from 2012 to 2015. However, due to a low rate (14.0%) of participation, the final number of participants was only 25,593.^[22]

Enteroscopy is the most intuitive method for the diagnosis of intestinal tumors. Rather than using a single colonoscopy for screening, as is standard practice in Europe and America,^[23,24] a combination of preliminary screens (risk assessment, stool examination, and others) and colonoscopy is recommended in China.^[25] Given the relatively scarce and non-uniform colonoscopy resources, single colonoscopy is not suitable for nationwide screening of rectal cancer in China. In Europe and the USA, early screening for rectal cancer has long been incorporated into the healthcare system. Due to medical insurance reimbursement issues involved in CRC screening, early screening for CRC has not been incorporated in the Chinese health care system thus far.^[19]

The universally acknowledged methods for rectal cancer staging are magnetic resonance imaging (MRI) and endoscopic ultrasonography (EUS). EUS can display high accuracy (80%–95%) in evaluating the depth of tumor invasion (T stage),^[26] particularly in the early stage. However, EUS has a poor performance in the evaluation of lymph nodes, with low overall sensitivity (55%) and specificity (78%).^[27] Compared to EUS, MRI provides superior imaging of advanced-stage rectal cancer and the interpretation is more intuitive.^[28,29] More importantly, the main advantage of MRI is the ability to identify positive lymph nodes, mesorectal fascia, and extravascular vascular invasion.^[30] High-resolution MRI is considered to be the best method for assessing the involvement of the circumferential margin in rectal cancer (accuracy: 0.932; sensitivity: 0.838; and specificity: 0.956).^[31] Therefore, National Comprehensive Cancer Network,^[32] European Society for Medical Oncology,^[33] and the clinical diagnosis and treatment guidelines of CRC in China (2017 version)^[34] all recommend MRI as the optimal imaging method for pre-operative diagnosis and staging of rectal cancer.

Surgical Treatment

In China, CRC surgery is performed in hospitals above the county level. However, quite a number of physicians probably do not provide standardized surgical treatments. A survey on the mastery of clinical diagnosis and treatment guidelines of CRC in China (2017 version) found that one-quarter of clinicians exhibit less than 50% accuracy, with an average overall accuracy of only 67%. This indicates that one-third of clinicians do not have a thorough understanding of the diagnosis and treatment specifications.^[35] Some clinicians even perform surgery without a clinical staging of rectal cancer. These findings reveal that there is a need for Chinese clinicians to improve their understanding of the guidelines.

At present, surgical treatment is still the most important treatment for rectal cancer. In recent decades, colorectal surgery has gradually become established in China. With the continuous development of colorectal surgery, the diagnosis and treatment guidelines of rectal cancer in China are gradually aligning with the international standards. In 2010, the National Health Commission of the People's Republic of China authorized the Oncology Branch of the Chinese Medical Association to organize experts in the field of CRC to write the first clinical guideline of diagnosis and treatment for CRC in China (2010 edition).^[36] This has since been revised in both 2015^[37] and 2017,^[34] and the latest revision was completed in 2020. With the gradual standardization of the surgical treatment of CRC in hospitals across China, and the development of comprehensive treatment methods such as chemoradiotherapy, targeted therapy, and immunotherapy, the post-operative quality of life and prognosis of patients with rectal cancer have improved. Clinically, CRC is typically divided into stages I, II, III, and IV, according to the clinical staging guidelines of the American Joint Committee on Cancer (8th edition).^[38]

Early rectal cancer ($T_1N_0M_0$)

Endoscopic resection (endoscopic mucosal resection/endoscopic submucosal dissection) and local surgical resection are the primary treatments for early rectal cancer.^[32-34] Due to the unique anatomical characteristics of rectal cancer, many local excisions that cannot be achieved in colon cancer can be used for rectal cancer, such as transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS).

TEM

The use of TEM in the treatment of early rectal cancer was firstly reported by Gerhard Buess in 1983.^[39] TEM involves expanding the intestinal tract with an air pump, and the use of binoculars produces clear, enlarged, three-dimensional images, thereby improving the surgical field and operating space and producing an ideal surgical effect. TEM has many advantages and greatly simplifies surgery on middle and high rectal lesions, as well as accurate evaluation of the surgical margins.^[40] With improvements to the surgical platform, studies have shown that there is no statistical difference in the R0 resection rate, post-operative recurrence rate, or tumor complete resection rate between TEM and ESD.^[41,42] A retrospective study of patients with low-risk completely (>1 mm) resected carcinoma reported 5- and 10-year local recurrence rates of 6.6% and 11.6%, respectively, over a median follow-up time of 8.6 years.^[43] In patients with high-risk or incompletely resected carcinoma, the rates were 32.5% and 35.0% ($P = 0.006$). These findings suggest that complete resection is essential to reduce the risk of local recurrence.^[43] According to the Chinese TEM consensus,^[44] TEM is currently used primarily in the treatment of early rectal cancer with good histopathological features. As the early diagnosis of rectal cancer increases in China, research on TEM is also increasing. Zhang *et al*^[45] reported that multiple TEM surgeries can ensure the normal function of the anus, with unique advantages. Wu *et al*^[46] demonstrated a low rate of complications, while

maintaining therapeutic effects. However, due to the steep learning curve and expensive surgical instruments, TEM has not been widely used in China. Additionally, most studies on TEM are retrospective studies and there remains a lack of prospective clinical studies with large multi-center cohorts.

TAMIS

TAMIS was developed in 2010 and is based on single-incision laparoscopic surgery. The indications for TAMIS are similar to those for TEM, and it is mainly used for the resection of benign and early middle- and high-rectal cancer.^[39] In addition, TAMIS-TME based on the TAMIS platform can also be used in some advanced rectal cancers (T_{2-3}) with increased systemic complications and no tolerance for surgery. The advantage of TAMIS is that the operation time is short and the cost is lower than that of TEM, but it cannot provide three-dimensional images for visualization, so doctors need to have extensive experience in laparoscopic operations.^[40] Studies have shown that the local recurrence rate of rectal cancer after TAMIS surgery is 4.3%, and the post-operative complication rate is 7.4%.^[47]

Locally advanced rectal cancer (LARC) ($T_{2-4}N_{0-2}M_0$)

Neoadjuvant therapy

Neoadjuvant chemoradiotherapy (nCRT) has a key role in the treatment of locally advanced mid-low rectal cancer, and has demonstrated efficacy in improving the R0 resection rate, anal preservation rate, and local control rate of tumors.^[48] In both national and international CRC guidelines, nCRT is the recommended treatment for patients with locally advanced low rectal cancer (IA).^[32-34] The classic neoadjuvant treatment is pre-operative concurrent chemoradiotherapy, which is divided into a long course (50.4 Gy/25 f)^[49] and a short course (5 Gy \times 5).^[50] These two radiotherapy methods are widely used throughout the world. In 2015, Gu *et al* achieved a high level of efficacy with a modified short course of 30 Gy/10 f based on pre-determined levels of tolerance to a long course of pre-operative chemoradiotherapy among the Chinese population.^[51]

Studies have found that 15% to 20% of rectal cancer patients have no pathological residue after nCRT, that is, they have achieved pathologic complete response before receiving radical surgery.^[52,53] In 2004, a Brazilian cohort consisting of 265 patients with LARC who received nCRT reported that 71 patients (26.8%) achieved clinical complete response (cCR). They additionally reported that cCR patients demonstrated good long-term survival regardless of the treatment strategy that was adopted, thus initiating the "watch and wait" or "W&W" strategy.^[54] In 2018, the results from the International Watch & Wait Database, including clinical data from 880 W&W patients from 47 participating institutions in 15 countries, showed that the 5-year OS of W&W patients that achieved a cCR after nCRT was 85%. Additionally, the 2-year local regrowth rate was 25% and 88% of the regrowth tumor could be resected with R0 by salvage TME surgery.^[55] As early as 2012, Gu *et al*^[56] registered a

clinical study of W&W after nCRT for LARC (ChiCTRTRC-12002488); the preliminary results were reported at the annual American Clinical Oncology meeting in 2017 and we have recently updated the data (not yet published). The study contains a total of 84 patients with cCR and has an average follow-up time of 34.8 months. The total recurrence and metastasis rate of the surgical group was 15.4% (4/26) and the W&W group was 18.9% (11/58). The OS rate was not statistically different between the two groups, indicating that patients with cCR after nCRT do not benefit from surgery.

With the W&W strategy gaining in popularity, more pre-operative neoadjuvant treatment models aimed at improving cCR rates are being explored. In China, the FOWARC^[57] study added oxaliplatin and the CinClare study^[58] added irinotecan during nCRT. These studies, as well as the study of total neoadjuvant treatment mode carried out by the Memorial Sloan-Kettering Cancer Center,^[59] have demonstrated that these pre-operative higher intensity combined chemotherapy regimens can improve the rates of cCR. In addition, extending the interval time after nCRT can also improve the cCR rate. Hupkens *et al*^[60] reported that 90% of patients evaluated as near cCR 8 to 10 weeks after the end of radiotherapy met the cCR standard when re-evaluated 12 weeks later. Given the limited number of patients that can potentially benefit from nCRT, it is critical to identify the molecular markers that predict the effectiveness of nCRT. Gu *et al*^[61-65] reported a correlation between single molecular markers (human epidermal growth factor receptor-2, phosphatidylinositol 3-kinase), microsatellite instability molecular phenotype, gene diversity, and chemoradiotherapy sensitivity of rectal cancer. However, it is not yet clear that any of the molecular biomarkers that predict the efficacy of pre-operative chemoradiotherapy can be used in the clinical setting.

Total mesorectal resection (TME)

TME was first reported by Heald *et al*^[66] in 1982 and introduced to China in the 1990s. A study conducted by the Shanghai Ruijin Hospital found that, compared with traditional surgical procedures, TME reduced the local recurrence rate from 9.09% to 3.95%. Additionally, the overall 5-year survival increased from 67.86% to 78.58%.^[67] In recent years, guidelines in both China and other countries have recommended TME as the first choice for rectal cancer surgery. Given the influence that the quality of the TME operation has on prognosis, a German research group evaluated the resection quality of 1152 surgical specimens and studied the effect on clinical outcomes. They found that the 3-year disease-free survival rates of patients with TME resection reaching the mesorectal plane (complete resection), intramesorectal plane (near complete resection), and muscularis propria plane (incomplete resection) were 75.9%, 68.4%, and 67.2%, respectively. The cumulative incidences for local recurrence were 3.3% for complete resection, 4.8% for near complete resection, and 12.0% for incomplete resection. For distant recurrence the rates were 19.7%, 25.5%, and 27.6%, respectively, while the 3-year OS rates were 90.3%, 85.1%, and 67.2%, respectively.^[68]

Minimally invasive surgery

Laparoscopic rectal cancer surgery has been performed in China for nearly 20 years. To the best of our knowledge, laparoscopic colorectal surgery was first used in clinical practice in China in 2001.^[69] In 2004, Zhou *et al* from the West China Hospital published a randomized controlled trial (RCT) study of radical laparoscopic surgery for rectal cancer, reporting that laparoscopic surgery can significantly reduce blood loss during the operation, shorten the length of hospitalization, and accelerate the recovery of bowel function compared with open surgery.^[70] A study conducted by the Fudan University Cancer Hospital indicated that laparoscopic TME can significantly increase the sphincter-preserving rate compared with open TME.^[71] An RCT study from the UK found that laparoscopic surgery for rectal cancer patients without tumor invasion of adjacent tissues was as safe and effective as open surgery.^[72] The short-term and long-term prognosis of patients undergoing laparoscopic surgery were similar to those who underwent open surgery.^[73,74] According to the Chinese Colorectal Cancer Database, in 2019, the proportion of colorectal laparoscopic surgeries performed was 56.7% in China,^[75] similar to the UK (60%), as well as Germany, Canada, and other countries.^[72,76] In 2010, Wang *et al* performed the transvaginal radical resection of rectal cancer and proposed the concept of Natural Orifice Specimen Extraction Surgery.^[77] The surgical specimen resection is performed intra-abdominally, then the specimen is extracted by opening a hollow organ that communicates with the outside of the body, including anus, vagina, or mouth. It has the advantages of avoidance of abdominal wall incisions as well as reduction of abdominal dysfunction.^[78] In June 2009, to the best of our knowledge, the first low rectal resection in China by the da Vinci robotic surgical system was reported.^[79] However, due to the advanced requirements for both operators and equipment, as well as the high cost of the surgery, robotic surgery remains difficult to carry out widely in some undeveloped areas of China.^[80]

Cylindrical rectal dissection

Cylindrical rectal dissection was first reported by Holm from the Stockholm Karolinska Hospital.^[81] Different from the traditional surgical techniques for rectal cancer, the cylindrical rectal dissection in the prone position shapes the specimen into a cylinder without a narrow waist, increases the resection volume of the peripheral tissues of the distal rectal cancer, and reduces the positive rate of the circumferential resection margin and the rate of intestinal perforation during the operation. Wang *et al*^[82] conducted the cylindrical abdominoperineal resection (CAPR) of rectal cancer in China. An RCT study in China showed that compared with traditional abdominoperineal resection operations, patients who received CAPR experienced reduced surgical time for the perineal portion ($P < 0.001$), less intraoperative blood loss ($P = 0.001$), and improved local recurrence ($P = 0.048$); however, there is an increased risk of a larger perineal defect ($P < 0.001$) and increased incidence of perineal pain ($P < 0.001$).

Transanal total mesorectal excision (TaTME)

In 2010, Chen *et al*^[83] took the lead in conducting the TaTME surgery in China and published an article on the treatment of rectal cancer by TaTME. At present, many hospitals in China have carried out this type of surgery. A matched case-control study by Chen *et al*^[84] found that compared with laparoscopic surgery, TaTME not only achieved identical circumferential margin status without compromising other operative and quality parameters but also benefited patients by achieving a longer distal margin. And a study carried out by Law *et al*^[85] indicated that the operating time was significantly shorter (254 *vs.* 170 min, $P < 0.05$) and the blood loss was less (50 *vs.* 150 mL, $P = 0.002$) in the TaTME compared with robotic surgery. Chinese consensus on transanal endoscopic surgery (2019 version) was officially released at the 2019 Annual Meeting of Surgeons of Chinese Medical Association. The definition of TaTME operation was clarified, and the indications of TaTME operation, including benign lesions such as rectal lesions of familial adenomatous polyposis, and malignant tumors such as middle and low rectal cancer, were further illustrated. At the same time, the five basic principles of taTME, including sterility, tumor-free, resection scope and quality control, specimen extraction method, as well as digestive tract reconstruction, were elaborated in detail. And the solutions for complications of taTME such as anastomotic leakage, urethral injury, and CO₂ embolization were also proposed.^[86] However, a Norwegian study that enrolled 110 patients with rectal cancer treated with taTME and followed them for 11 months reported a local recurrence rate of 9.5%, far higher than the previously reported local recurrence rate of 3.4%.^[87] As a result, Norway called for taTME to be stopped.

Lateral lymph node dissection

In cases where pre-operative examination indicates the presence of lateral lymph node metastasis, the majority of European and North American countries recommend TME surgery combined with radiotherapy and chemotherapy, while Asian countries such as China and Japan primarily use intra-operative lateral lymph node dissection. The European and American assessment is that lateral lymph node metastasis is a systemic disease requiring systemic treatment, and lateral lymph node dissection may increase the possibility of urogenital complications.^[88] However, the latest research shows that the standard nCRT recommended in Europe and America may not be sufficient to prevent local recurrence in patients with advanced low rectal cancer (cT₃/T₄) and lateral lymph node short axis greater than or equal to 7 mm.^[89] A meta-analysis suggested that lateral lymphadenectomy did not improve the 5-year survival of patients, and the incidence of urinary and sexual dysfunction was even higher than that of TME without lateral lymphadenectomy.^[88] Another meta-analysis also indicated that TME with lateral lymph node dissection might cause more complications compared with TME on rectal cancer patients.^[90] Kusters *et al*^[91] compared the prognosis of low rectal cancer patients in Japan and the Netherlands, and found that the incidence of presacral recurrence in patients

undergoing lateral lymphadenectomy was reduced (0.6% compared with TME (3.2%) and radiotherapy + TME (3.7%)). Ito *et al*^[92] also found that mesorectal excision with lateral lymph node dissection was not associated with a significant increase in the incidence of urinary dysfunction and that urinary dysfunction was associated with tumor location and blood loss in an RCT study. A meta-analysis of clinical studies on lateral lymphadenectomy of low rectal cancer in China found that lateral lymphadenectomy prolongs the operation time, increases the amount of bleeding, and increases the risk of post-operative complications such as sexual dysfunction, but that it has a positive impact on reducing the local recurrence rate and improving the 3- and 5-year survival.^[93] Whether lateral lymphadenectomy is necessary in rectal cancer surgery remains controversial in China.

Advanced rectal cancer (T₁₋₃N_{any}M₁)

The liver is the most common site of metastasis for CRC, occurring in approximately 50% of patients. Liver metastasis is divided equally between synchronous and metachronous metastases, with each occurring in about 25% of CRC patients. Colorectal liver metastases (CLM) is also a major cause of mortality in CRC patients.^[94] Rectal cancer (34.9%) is associated with a higher incidence of liver metastasis compared to colon cancer (26.7%).^[95] The 5-year OS is less than 5% for patients with inoperable metastatic tumors. However, similar to CRC, an R₀ resection of both the primary and metastatic lesions greatly improves survival.^[96] Adam *et al*^[97] analyzed data from 10,000 CLM patients and reported that the 5-year OS of CRC patients with hepatectomy is approximately 40%. The 5-year OS approached 55% for CLM patients with hepatectomy in the MD Anderson Cancer Center.^[98] In China, a retrospective study of 1613 CLM patients admitted to the Fudan University Zhongshan Hospital reported a 5-year OS of approximately 37% for CLM patients with hepatectomy.^[99] However, these operations call for a dedicated multidisciplinary team (MDT).^[100] The Department of Colorectal Surgery at Peking University Cancer Hospital developed an MDT treatment model in 2005, which significantly improved the 5-year OS of CRC patients (77.23% *vs.* 69.75%).^[101]

Currently, surgery remains the best treatment for CLM. Pawlik *et al*^[102] found that patients with negative margins of 1 to 4 mm, 5 to 9 mm, and ≥ 1 cm after hepatic resection for CLM all had similar overall recurrence rates. An R₀ resection can also be performed on surgical margins of 1 mm. Local removal is recommended, with a safe margin of 1 mm for each lesion. This operative principle is also called the parenchymal sparing hepatectomy. With the improvement of surgical techniques and the concept of translational therapy, many initially unresectable CLM patients can now undergo R₀ resection. These treatments mainly include systemic chemotherapy, radiofrequency ablation, hepatic artery infusion and associating liver partition and portal vein ligation for staged hepatectomy (ALPPS).^[103,104] Currently, due to the high risk, high incidence rate of complications, and uncertainty of the effects on long-term survival, few patients are truly suitable for ALPPS in China.^[105]

Compared to liver metastases, lung metastases accounted for 32.9% of all metastatic CRCs.^[106] Similarly, rectal cancer also has a higher risk of developing lung metastases compared to colon cancer.^[107] According to the expert consensus on the multidisciplinary treatment of CRC with lung metastases (2019 edition) in China, treatment strategies for patients who initially have resectable lung metastases mainly include R₀ surgery, stereotactic body radiation therapy, and ablation therapy. Surgery is considered to provide the clearest benefit to patients. After resection of the intrapulmonary lesions, the 5-year OS is 35% to 70%. It is recommended that aggressive surgical resection should be conducted on patients with resectable lung metastases. Radiotherapy and ablation therapy can be considered as alternative measures for patients who are not suitable for surgery due to tumor site, expected residual lung function, patient tolerance, or patient willingness.^[108]

Peritoneal metastases accounted for 4% to 7% of all metastatic CRCs.^[109] Peritoneal metastasis is associated with end-stage CRC, and has a worse prognosis than cancer at other sites of metastases. At present, peritoneal metastasis is mainly treated by cytoreductive surgery plus hyperthermic intraperitoneal chemotherapy, which improves the prognosis of these patients to some extent.^[110] However, these therapies are not widely used in China due to the complicated nature of the surgeries and the high incidence rate of complications.

In summary, the treatment level of rectal cancer in China still lags behind that in developed countries, especially in the USA. With the continuous standardization and internationalization of China's comprehensive treatment based on surgical treatment, as well as the implementation of early screening nationwide, the inflection point of the rising incidence and mortality of rectal cancer will appear in the near future in China.

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Conflicts of interest

None.

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