

# État actuel de prise en charge chirurgicale du cancer du rectum en Chine

## Current Status of Rectal Cancer Treatment in China

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### Mots clés

- ◆ Cancer du rectum
- ◆ Cancer colorectal

### Résumé

Le cancer colorectal (CCR) est le quatrième cancer le plus fréquent en Chine. Pour des raisons économiques, un registre national du cancer colorectal n'a pas été mis en place et un programme de dépistage à grande échelle n'a encore été mis en œuvre. Par conséquent, les données statistiques exactes concernant l'incidence du CCR couvrant l'ensemble du pays ne peuvent être fournies.

En Chine la plupart des hôpitaux des grandes villes ainsi que les hôpitaux provinciaux sont en mesure de prendre en charge les patients atteints de CCR. Mais, en raison des disparités économiques, des conditions médicales et des niveaux de compétences, il y a une grande variation dans les traitements. La plupart des oncologues prennent leurs décisions thérapeutiques en se basant sur les recommandations du National Comprehensive Cancer Network (NCCN) bien que certaines recommandations nationales soient maintenant possibles.

Le 11 octobre 2011, le ministre chinois de la santé a publié un guide national des recommandations des bonnes pratiques cliniques du traitement du CCR. Ceci devrait permettre une certaine conformité dans le traitement du CCR à l'échelon national et permettre que des soins de meilleure qualité soient délivrés en particulier en zone rurale.

En raison des problèmes de langues, la recherche concernant le CCR en Chine a un impact limité dans la littérature internationale et des difficultés de compréhensions de la situation actuelle du pays. Les chirurgiens chinois urgentistes spécialistes du CCR ont besoin d'échanger leurs connaissances avec leurs collègues internationaux. Dans cette présentation la situation actuelle concernant le traitement du cancer du rectum sera abordé.

### Keywords

- ◆ Rectal cancer
- ◆ Colorectal cancer

### Abstract

Colorectal cancer (CRC) is the fourth most common carcinoma in China. For economic reasons, a national colorectal cancer registry system has not been established and a large scale screening program has not yet been implemented. Therefore, accurate statistical data concerning the incidence of colorectal cancer covering the whole country cannot be obtained. In China, the majority of hospitals in central cities and even in county hospitals are able to provide medical care for CRC patients. Due to socioeconomic disparities, medical conditions and skill levels, there is a wide variation in the treatment. Most oncologists make their clinical decisions based on the National Comprehensive Cancer Network (NCCN) guidelines although some domestic guidelines are now available. In October 11, 2011, the China Ministry of Health released the National Guideline of colorectal cancer treatment. This will give a degree of standardization of the treatment of CRC nationwide and will ensure that higher quality care will be available, especially in rural areas. Owing to language difficulties, research on CRC in China has only had a limited exposure in the international literature, due in some part to lack of understanding of the current position in the country. Chinese colorectal surgeons urgently need to exchange their knowledge and experience with international colleagues. In this article, the current situation regarding surgical treatment of rectal cancer in China is summarized.

## The incidence of colorectal cancer in China

Colorectal cancer (CRC) in China has features related to its socio-economic situation as a developing country. The incidence of rectal cancer is higher than colonic. Retrospective data from local regions of Shanghai, Beijing, and Guangdong demonstrate that rectal cancer accounts for 59.4% -71% of the total population of about 80,000 colorectal cancer patients (1

-5). Qing compared the site and incidence of colorectal cancer between Americans (690 cases) and Chinese patients (870 cases) and the results showed the Chinese patients are more likely to suffer from distal colonic or rectal cancer, while the Americans, especially males, are more prone to proximal colon cancer (1). A proximal shift has since been observed in the past few decades in China (2-4). Compared with developed countries, the onset of CRC is at a younger age. In one study 6.1% of colorectal cancer occurred before the age of 30 and in another there was an increase of 2% per year in the incidence

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of patients of proximal colon cancer in patients aged between 35 to 44 years (2,5). The peak of CRC incidence emerged between 61-70 years (1-3), however, the median age at diagnosis postponed 7 years in male (from 50 to 57), and 8 years in female (from 52 to 60) in the past two decades (4,5). The sex ratio of CRC in Europe and America (6), may not be translatable to China where the data are inconsistent. Li reported a predominance of male patients and a study from Shanghai suggested that the gender ratio might be age-related (7). China still lacks a national large-scale cancer screening system. Early detection of colorectal cancer through screening is still not available in some remote areas. In addition the national cancer registration system is not well developed. Registration and reporting of CRC are carried out by tumor registration centers mostly in urban areas such as Beijing, Shanghai, and Guangdong. A nation-wide screening system for CRC is expected in the near future.

## Staging of rectal cancer

Strategy for the treatment of colorectal cancer (CRC) has undergone significant development regarding preoperative investigation and staging. The use of spiral CT and transrectal ultrasound has been well accepted in China for preoperative assessment of the locoregional and distant disease. Retrospective studies have revealed that the accuracy of transrectal ultrasound is superior to spiral CT for T staging, while spiral CT is superior for N staging (8-10). More recently high-resolution MRI has been used for preoperative T staging and to determine involvement of the mesorectal fascia by the cancer. The overall accuracy of T staging has been reported to be 85.1% with an increased sensitivity for more advanced T stages (T2, T3, T4; 70%, 90.5%, 100%). The accuracy of prediction of involvement of mesorectal fascia was 88% (8,11).

The multimodal preoperative evaluation (MPE) system is a novel strategy for surgical decision making, incorporating transrectal ultrasound (TRUS), 64 multi-slice spiral computer tomography (MSCT), and serum amyloid A protein (SAA). This has been used in a study of 225 CRC patients to assess its value for staging (12). The Physiological and Operative Severity Score for the enumeration of Mortality and Morbidity (POSSUM) system has also been used to assess the immediate postoperative prognosis (13). The Chinese Ministry of Health endorsed the 7th edition of the AJCC guidelines on diagnosis and treatment and recommended that preoperative CT scan or MRI, especially for rectal cancer is essential for pretreatment staging of CRC (14).

## Local excision of early-stage CRC

Early diagnosis of cancer is poorly carried out in China, as indicated by detection rates of 1.7% to 26.1% for T1 and T2 lesions (15,16). No consensus for the definition of "early stage" colorectal cancer has been reached, nor for the most appropriate operation. The NCCN guidelines suggest that local excision should be limited to stage T1 lesions located within 8 cm of the dentate line without apparent lymph node or distant metastasis (17). However, the surgical indications for local excision in early rectal cancer are not always in compliance with the guidelines. Thus in a study from the Chinese Academy of Medical Sciences Cancer Center of 47 patients local excision was performed on both stage T1 and T2 tumors, with respective 5-year survival rates of 94.4% and 83.3% and a recurrence rates after excision of T2 cancer of 14.9% (16). Another study from Beijing Union Medical College Hospital reported 106 patients (including 48 T1 and 26 T2 lesions) having local excision in the past 25 years with an overall local recurrence of 17.0% and a 5-year survival rate of 86.7% (15). Patients with stage T2 and an ulcerating tumor experienced a

higher recurrence rate after local excision, despite the use of postoperative chemotherapy and radiotherapy in some cases (18,19). Transanal endoscopic microsurgery (TEM) has been commonly used in China, especially for those patients with a stage T1 and histologically well-differentiated cancer (20). TEM in well selected patients resulted in less than 5% local recurrence rate, and a 5-year survival rate of approximately 100%, similar to the results of major radical excision (19-21). In addition to perianal local excision, there are reports on transvaginal resection and excision by the sacrum with low rates of recurrence and complications (15,22). These methods might be used as an alternative strategy to abdominoperineal resection or low anterior resection in very carefully selected patients.

## Advanced rectal cancer

### Neoadjuvant therapy

Surgical excision of CRC has been widely carried out in almost all hospitals in China including those at county-level. In accordance with international guidelines such as derived from the NCCN or the European Society for Medical Oncology (ESMO), Chinese guidelines advocate neoadjuvant chemoradiotherapy for advanced rectal cancer. The concept of preoperative chemoradiotherapy has been accepted among Chinese doctors, but standard preoperative treatment could only be implemented in some teaching hospitals and cancer hospitals in urban cities. Even though long course preoperative radiotherapy has been prescribed for locally advanced rectal cancer, the compliance rate has been low due to the long period of preoperative treatment, which usually takes around three months. Some hospitals have, therefore, made adaptations to the dose fractionation regime. For example at Peking University Cancer Hospital have used preoperative radiotherapy to a total dose of 30 Gy in 10 fractions with a two week interval to surgery and have demonstrated improved patient compliance with not increase in morbidity (23). This dose fractionation regime has been recommended by the Chinese Anti-Cancer Association and is widely used by the Colorectal Cancer Treatment Society.

### Total mesorectal excision (TME)

TME surgery was introduced to China by Dr Bill Heald in the 1990s, and studies reporting the results of this technique were published few years later. TME was initially carried out in Shanghai Ruij in Hospital where Yu et al performed it in 306 patients with rectal cancer. The local recurrence rate was 6.7% and long-term overall survival rate was 92.6% (24). In another report the local recurrence rate after TME was around 6%, consistent with results from Europe, but long-term survival was not improved (25).

### Minimally invasive surgery including robotic surgery

Since the first successful laparoscopic colectomy (26), this form of minimally invasive surgery has been widely carried out in China over the past 20 years. The first laparoscopic TME was reported in 2001, and in a series of 105 patients with rectal cancer lying at a mean of 4 cm from the dentate line, the 5-year local recurrence and survival rates were 8.9% and 81.3% (27). A large-scale follow-up study of laparoscopic resection of 579 cases of rectal cancer reported tumor-specific 5-year and 10 year survival rates of 70% and 45.5% (28). A study comparing open with laparoscopic TME in 612 cases showed that there was hardly any difference in 5 year local

recurrence and overall survival rates indicating that the latter was as radical as the former (29). With regard to the length of bowel resected, lymph node dissection and retrieval, survival and recurrence rates and the integrity of the mesorectum, properly conducted laparoscopic surgery resulted in a clinical outcome similar to open surgery, but significantly reduced the administration of postoperative narcotic drugs, leading to a faster recovery of the gastrointestinal tract, bladder function and earlier discharge (27,30-32).

In China, the first robotic-assisted colorectal surgery using the Leonardo da Vinci minimally invasive technique took place about 5 years after it had been approved by FDA in 2000. Few papers have been published owing to its high cost and limited application. A study of 15 patients undergoing rectal operations by robotic surgery showed a similar short-term outcome with no complications compared with laparoscopic surgery (33). Meta-analysis comparing laparoscopic surgery and robotic surgery has demonstrated the latter method to benefit from less blood loss, shorter hospital stay, lower rate of intraoperative conversion, especially when TME principle was followed (34). Nevertheless, due to the lack of long-term outcome data, the place of Robotic surgery in China still needs further investigation.

### Lateral lymph node dissection

The value of lateral lymph node dissection (LLND) is still controversial. Freidin and Grinnell thought that the metastasis along this path was only 2% and the dissection was unnecessary (35). Studies from Japan indicated that the lateral metastasis rate was between 12-24% (36-39). Thus, lateral lymph node dissection is now recommended for advanced rectal cancer by Japanese guidelines. However, a recent multicentre trial of 351 patients showed that the lateral lymph node metastatic rate was 7%, and no difference was found between patients who underwent LLND and those who did not (40). In China, the rates of lateral lymph node metastasis were reported to be higher than in western countries (7.1% -19.1%) (41,42). Conventional lymph node dissection was implemented by Chinese colorectal surgeons and lateral lymph node metastasis was demonstrated as an independent factor for a poorer prognosis (43). However, there are studies questioning the benefits of LLND due to the increased rate of complications including sexual and urinary dysfunction (44).

### Total pelvic exenteration (TPE)

For advanced lower rectal cancer, TPE has been demonstrated to be the only effective treatment. Studies from Japan have demonstrated 5 year survival after TPE to be around 40-50% (45-47) and similar results have been reported from Taiwan (48). A retrospective study from China reported a 5 year survival rate of 30.7% (43). TPE leads to better outcome as long as careful patient selection is strictly applied.

### Preservation of the pelvic autonomic nerves

Radical excision has greatly improved patients' outcome, however, it inevitably results in increased complications, such as postoperative bladder and sexual dysfunction and other serious problems affecting quality of life. Based on the recognition of the detailed anatomy of the pelvic autonomic nerves, Pelvic Autonomic Nerve Preservation (PNAP) was first proposed by a Japanese group (49,50) and this was adopted in China the late 1980s. Autonomic nerve preservation has been applied to patients with Stage IIIB tumors or less where there is no nerve invasion. Studies appear to have demonstrated the advantage of this technique with resultant urinary (5.4%) and sexual dysfunction of around 5% and 22% (male 0 and 30% 9 female) (51,52).

### Cylindrical rectal dissection

The importance of achieving a so called cylindrical dissection when performing an abdominoperineal resection, has been emphasised by Holm. This procedure may reduce circumferential margin positivity, intraoperative perforation and local recurrence (53). In a small Chinese study cylindrical dissection was combined with preservation of the pelvic floor to preserve anal function with good results (54).

### Adjuvant chemotherapy

Adjuvant chemotherapy may be important in reducing the incidence of local recurrence and metastasis. In China, adjuvant chemotherapy has been conventionally conducted by surgeons and has usually been given to patients with stage pT3 lesions. A small number of patients receive chemotherapy from medical oncologists. Following NCCN guidelines, fluoropyrimidine has been the mainstay of choice of chemotherapy in China. Oxaliplatin, capecitabine and irinotecan are all available and have been frequently prescribed in recent years.

### Radiotherapy

Postoperative radiotherapy is still used in some units in China, even though there is a large body of evidence to show that preoperative neoadjuvant chemoradiotherapy is superior. Some studies in the early 1990s showed that postoperative radiotherapy and chemotherapy significantly improved survival rate, and reduced local recurrence for patients with stage II-III resectable rectal cancer compared with surgery alone, (55,56) but these have since given way to its replacement by preoperative radiotherapy other than in a few clinical circumstances. Image-guided radiation therapy (IGRT) may be a more effective way to deliver this treatment and there are some units in China using this technique (58).

### The Multidisciplinary Team (MDT)

The introduction of the MDT dates back to the early 2000s (57) and is now widely accepted among those treating rectal cancer. A retrospective study of 263 cases from Beijing Cancer Hospital reported that as a result of MDT discussion the treatment was altered in over half of patients which may have led to a better long term outcome (58).

## Colorectal surgeon training in China

### Specialist registration

Training of a western colorectal surgeon usually includes about 5 years of general surgery residency and two years of specialized colorectal training. A qualified colorectal specialist therefore need at least 11-12 years of medical training including the time spent in medical school. In China, however, there is as yet no academic registration system for colorectal specialization and in the light of this colorectal surgical training at present is part of general surgery. This can be relatively little; for example at Peking University, surgical residency training includes a clinical rotation in digestive tract surgery for only weeks to months. In order to meet the core competence required for colorectal surgery, more training needs to be implemented in the special field of colorectal surgery.

## Academic associations and Continue Medical Education

There are several academic organizations dedicated to colorectal surgery in China, including the Anorectal Surgery Group of the Chinese Medical Association, the Colorectal Cancer Society of the Chinese Anti-Cancer Association, and the newly formed Chinese Association of Anorectal Surgeons. These organizations hold regular academic conferences and carry out professional training. Continuing education mainly for residents and fellows. The training programs are tailored to meet individual levels and residents have to fulfill the criteria for training courses. There is, however, virtually no further training or academic assessment for senior professionals.

Rapid progress has been made in China in the diagnosis and treatment of colorectal cancer. However, there is still a gap between China and well-developed countries. This is largely due to the following reasons: (1) systemic screening of CRC has not been carried out; (2) standard treatment, including pre-operative staging and preoperative neoadjuvant therapy, is not widely conducted; (3) postoperative adjuvant therapy has not yet been standardized; (4) MDT is only achieved in a few hospitals.

## Discussion

Reviewers and Professor Daniel Jaeck asked some questions

1) The series applies the area of Shanghai, Beijing and Guangdong who are the most favored in China.

Have you got a commentary upon it?

**Reply**

The incidence of colorectal cancer (CRC) has been certainly arising in the past decades. However, due to the lack of national cancer registration system, the data we showed in the paper was limited. So far, the incidence data was obtained from retrospective analysis, and therefore scattered and incomplete. Data from the most favored cities (Beijing, Shanghai, Hong Kong and Zhongshan (a large city from Guangdong), see attached files from IARC) shares certain similarities: firstly, a trend is emerging that CRC ranks the 1st among the gastrointestinal malignancies in terms of incidence; secondly, recent data implies an increase of colon cancer as well as a decrease of rectal cancer. There has been no quick answer to this phenomenon. One possible explanation is that people from modernized cities share the resemblance of life-style, both in China and western world. Factors, such as food, body weight, smoking, etc. might be involved in the occurrence of this disease.

2) It is interesting to note that the rectal cancer represent 60 to 70% of colorectal cancer in China.

Why? More easy to diagnose?

**Reply**

There are a few hypothesis to explain the high rates of rectal cancer in China.

First, it is true that the diagnosis of rectal cancer depends less on equipment, compared with colon cancer. So far, the digital rectal examination (DRE) is still one of the golden principles for rectal mass, and the DRE can be performed by experienced doctors easily. Meanwhile, colonoscopy seems essential to identify colon tumor, which requires more advanced platform and therefore more expensive.

Secondly, from the perspective of patients, the clinical manifestations of rectal cancer seems more direct and characteristics, which would easily draw attention. Rectal bleeding as well as tenesmus are the most common complains for rectal cancer. Nevertheless, for colon cancer, the change of bowel

habit occurs majorly, which might be naturally ignored, or regarded as indigestion.

3) The beginning of colorectal cancer is more premature in China compare of the number in Europe or in USA.

What hypothesis?

**Reply**

The "premature" colorectal patients might be explained as follows:

-First, in the review, we mentioned a nearly 10 year difference of median age in the CRC epidemiology in China (peak incidence 51-60), compared with western world (peak incidence 61-70). The high proportion of young CRC patients shown by our review has been an important characteristic of CRC in China, but it was difficult to compare data regarding age. Some papers employed the cutting age as "40", or "50".

-Secondly, there has been an increase in the median age of CRC patients in the past decades, from around 50 to around 56, which is more similar to the western world. Therefore, it is possible the previous data was limited to the areas of resource.

4) Peri rectal lymphnodes seem more frequent in China (7 to 20%) compare to occidental countries.

What explanation can be suggested?

**Reply**

The implement of early detection of CRC is still incomplete, which is a shame in such a large country like China, compared with western world. Thereafter, majority of the patients are diagnosed as locally advanced rectal cancer, with higher percentage of lymph-node involvement; on the other hand, more than half of the patients are diagnosed as early rectal cancer (without lymph node metastasis) in developed countries, such as France, Great Britain, USA, Japan, etc.

5) Adjuvant treatments (radiotherapy - chemotherapy) seem more frequently used compare to neo adjuvants.

Why?

**Reply**

With the continuous medical education by Chinese Medical Association, together with the spread of certain guidelines, like NCCN and ESMO, there has been increasing number of oncologists accept the idea of "comprehensive treatment" of rectal cancer. For mid-low locally advanced rectal cancer (LARC) (based on pre-operational staging), patients are supposed to obtain "neo-adjuvant chemo-radiation", followed by TME surgery, and adjuvant chemotherapy (based on post-operative pathology). However, it is true for those LARC, that neo-adjuvant chemo-radiation is not well accepted and performed due to several reasons. Firstly, there has been inadequate amount of radiological equipment as well as experienced radiologists in small cities or rural areas. Secondly, certain patients are in favor of adjuvant treatment (chemo, or radio-therapy) when told with "small percentage" of distant metastasis during neo-adjuvant treatment. Thirdly, neo-adjuvant treatment (especially radiotherapy) costs a large amount (around 6000 U.S dollars), and poor people could not afford.

6) Training of colorectal surgeons is assumed by many associations (Chinese Medical Association - Chinese Anti-Cancer Association etc...)

How the distribution of young surgeons in formation is made and how is estimated their level of competence?

**Reply**

At present, training of colorectal surgeons in China, is still lack of standard principle. Only a few specialized departments are named after "Colorectal Surgery", while the rests somehow belong to the gastro-intestinal surgery, or even general surgery. The standardized training in residents of colorectal surgery from U.S.A requires 5-6 years of specialized

rotations. The competence of these young surgeons are uneven. Experience from Peking University (Beijing Cancer Hospital) pioneered in China.

## Contributions

Both Jin Gu and Nan Chen are involved in the entire process of this paper, including design, acquisition of data, interpretation of data and manuscript writing.

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