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VIEWPOINT

Rectal Cancer in West China: Younger Onset, Poor Survival, and Poor Compliance

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Rectal cancer (RC) is one of the most common malignancies worldwide.[1] Because of the introduction and dissemination of screening tests, the improvement in treatment strategies, and good compliance with follow-up monitoring, the survival rate for patients with RC has gradually improved during the past decades.[2,3] However, obvious differences in reported oncological outcomes still exist between geographic areas due to economic level, medical imbalance, and the proportion of elderly population. The Chinese National Central Cancer Registry was established in 2002 and covers only 13% of the national population, in sharp contrast to 96% covered in the United States and nearly 100% in the United Kingdom. In addition, most of the registry-source centers were located on the "east coast" in the high-income areas of China, thus limited in terms of reflecting the national cohort.[4,5] Due to a relatively poorer economic level, a lower proportion of a well-educated population, and great lack of available medical resources, especially endoscopy, it is much more difficult to estimate the status of colorectal cancer in West China. Furthermore, the Chinese health care system differs considerably from those of developed countries in Europe, North America, and even East Asia. Most surgery is performed in the very limited tertiary centers, often overwhelmed by thousands of inpatients, such as the West China Hospital of Sichuan University. Thus, a single-center report from one of these hospitals is representative of the general status of RC care in these areas.

The current treatment guidelines distributed by the respective Chinese professional associations (National Cancer Center of China, Chinese Society of Clinical Oncology, Chinese Anti-cancer Association) are similar, in general, to the widely used National Comprehensive Cancer Network and European Society for Medical Oncology guidelines for RC.[6,7] Patients with clinical $T3N^+$ stage RC, those with a resectable tumor above $T3N^+$ stage, but who refuse neoadjuvant therapy, and those who have completed neoadjuvant therapy, undergo curative rectal resection according to the standards of total mesorectal excision. Patients with advanced disease (ie, $T3^+N^+$ and above) undergo neoadjuvant radiation accompanied by chemotherapy. Patients with lymph node metastasis or other pathological risk factors are recommended to receive adjuvant therapy. All patients are scheduled for periodic postoperative follow-up with CT and colonoscopy. The details regarding adjuvant therapy and surveillance are similar to those recommended by the National Comprehensive Cancer Network guidelines for rectal cancer.[6]

We retrospectively evaluated the clinicopathological characteristics, timing trends, status of neoadjuvant and postoperative treatment regimens, oncological outcomes, and follow-up information of patients with RC receiving curative resection in this second largest hospital in China from 2009 to 2019. We also aimed to evaluate the association between the compliance with treatment and follow-up with oncological outcomes. During this period, nearly 8200 patients with nonmetastatic RC received curative resection at our department, accounting for nearly 60% of colorectal cancers. In addition, 71.9% of these RCs were located below the peritoneal flexion. The tumor location was quite different than data from North America, Europe, and other countries in Eastern Asia.[3,8] The difference may be partly due to racial and ethnic disparities;

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however, selection bias still exists because the less technically demanding colon and upper rectal resections were more likely to be performed at local hospitals.[9] About 8.0% of patients with RC were younger than 40 years, and more than 25% of patients with RC were younger than 50 years, whereas less than 40% of the patients with RC were older than 65 years. However, the proportion of younger patients was much higher than that in developed countries, which might be related in part to center congregation, willingness to follow screening tests and treatments, and differences in genetic backgrounds, susceptibility, and dietary habits. Because of the high incidence of RC in the young population, health care providers should consider not only the "50 year" age criteria when determining the timing for screening endoscopy, but also the other risk factors related to the occurrence of RC.

The proportions of patients with stage II and stage III RC were 40.3% and 42.4%, which were much higher than the proportion of advanced RCs in developed countries. Further survival analysis showed that the 5-year overall survival rates for stage II and III RCs were 69.3%, and 46.9%, far lower than those in developed countries. According to the published data, the survival of patients with advanced RC has greatly improved, increasing from 45% in the 1970s to 70% in the 2000s for RC in the United States.[2] The popularization and application of RC screening programs, especially endoscopy, ensures that far more patients are diagnosed with precancerous or early-stage disease in the developed countries than those of others.[10] However, in China, the vast population, large geographical span, diverse cultures, and socioeconomic groups create wide disparities in cancer care. According to information from China Health Statistics Yearbook 2018,[11] although the number of hospitals in the eastern coastal and western regions are similar, the average number of high-quality tertiary hospitals in the western region is significantly lower than that in the eastern region (number of tertiary hospitals: 342 vs 619), and there are twice as many beds available in urban areas as in rural areas (6.24 vs 2.8 per 1000 inhabitants). The per capita health input costs in the western region are also much lower than those in the eastern region (3000 RMB Sichuan province vs 9000 RMB Beijing). Apart from these, adequate cancer care in China is also hampered by a shortage and uneven distribution of oncologists and qualified staff with rural areas having difficulty in attracting and retaining qualified health care providers. According to the Yearbook 2018,[11] there are 8.5 doctors or nurses per 1000 people in eastern China, compared with 2.8 per 1000 people in rural western China. The number of oncologists varies even more dramatically. Unlike patients who have cancer in Europe and North America, who experience several transfers from primary caretaker to specialist, patients in China are relatively free to choose their health care providers regardless of location. As a result, they tend to gather in large tertiary centers in urban cities. This trend also leads to overcrowding of renowned inner city facilities and prolonged times to examination and treatment, while also increasing the expenses for patients.[12] Compared with the difficulty of achieving a screening program, the lack of cancer awareness in the lay population is critical to early diagnosis and timely treatment. A considerable number of Chinese inhabitants never participate in routine medical checkups and are therefore diagnosed with late-stage disease. All these factors lead to the poor oncological outcome for patients with RC in China, especially West China.

Further survival associated analysis showed that only 39.6% of those patients with stage III RC completed full-course guideline recommended systemic chemotherapy or chemoradiation. The median time to initiate adjuvant therapy was 39 (interquartile range, 25–53) days after surgery. Table 1 shows compliance with recommendations for adjuvant therapy and with follow-up. Worse compliance with adjuvant therapy and follow-up both led to worse survival outcomes (Fig. 1). The 5-year overall survival rates for stage III RCs with decreasing levels of compliance with adjuvant therapy were 51.5%, 47.1%, and 42.2% ($p < 0.001$), whereas the 5-year overall survival rates for stage III RCs with decreasing levels of compliance with follow-up were 66.3%, 41.9%, and 39.9% ($p < 0.001$).

In Chinese communities, traditional and cultural factors have a significant effect on the treatment and survivorship of patients with cancer: factors such as fatalism, which is common in China, especially in comparatively undeveloped western areas.[12] Here, a great proportion of patients choose to give up once the diagnosis of a malignant tumor is confirmed. Another group of patients choose to receive only surgery, because they believe the treatment of chemotherapy and radiation will only bring harm to their body while not controlling the disease. In

TABLE 1. Compliance with adjuvant therapy and follow-up for patients with stage III rectal cancer

Variables	*Compliant*	*Partly compliant*	*Not compliant*
Adjuvant therapy (3476 at risk)	1376 (39.6) [a]	897 (25.8) [b]	1203 (34.6)
Follow-up (3476 at risk)	883 (25.4)	1564 (45)	1029 (29.6) [c]

The values displayed are number of patients (%).

[a] Completed full-course guideline-recommended systemic chemotherapy or chemoradiation.

[b] Chose oral fluorouracil or similar regimens only; refused recommended chemoradiation.

[c] No more than one follow-up within 2 years of surgery and no annual follow-up after 2 years.

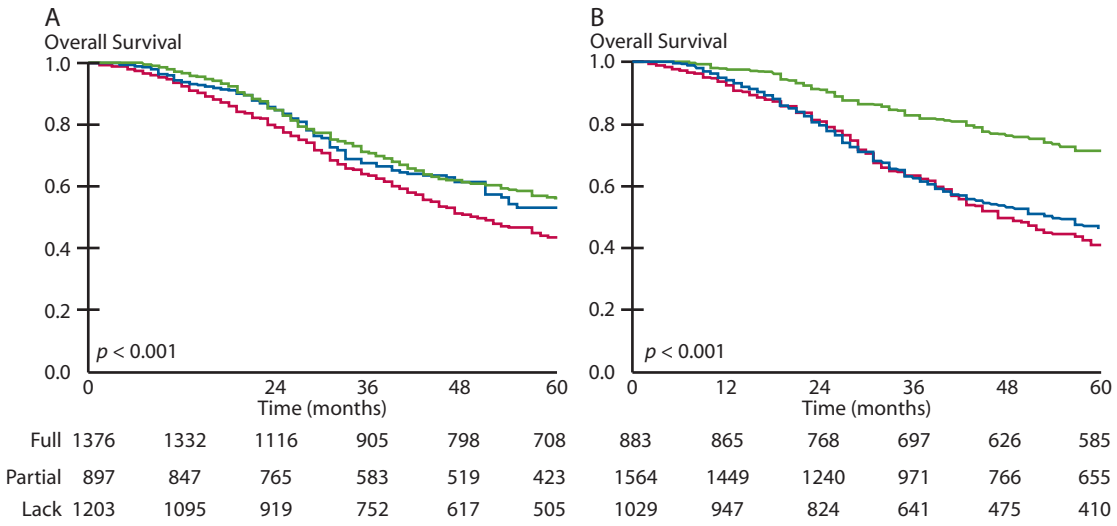

FIGURE 1. Kaplan-Meier plots illustrating the association between compliance with postoperative adjuvant therapy (A) and postoperative follow-up schedule and the rates of 5-year overall survival after curative rectal cancer surgery for patients with stage III rectal cancer (B). Green lines refer to full compliance, red lines refer to lack of compliance (defined as no more than one follow-up within 2 years of surgery and no annual follow-up after 2 years), and blue lines refer to partial compliance. In the case of adjuvant therapy, this refers to use of oral agents only and failure to follow recommendations for chemoradiation.

this belief, treatment of cancer is hampered by widespread perceptions that death is inevitable after cancer diagnosis and that the outcome is predestined, irrespective of medical intervention.[12] At the same time, a considerable number of patients with cancer often believe that traditional Chinese medicine can help to improve general well-being, relieve symptoms, and cure diseases. High-level evidence for the clinical efficacy of traditional medicine is still lacking. Understanding cancer fatalism and its role in China is important in understanding the choice of patients and in following clinical outcomes.

Some limitations of this study should be addressed. Selection bias exists because the "easier" cancers were more likely to receive treatment locally, whereas those patients with critical disease or those with complications were prone to travel to our center. Because the national cancer registry is in the process of gradual improvement, data concerning patients receiving adjuvant therapy and follow-up at local hospitals was partially lost, especially data of those who changed contacts after discharge. In conclusion, there is much work needed to improve the oncological outcome for RCs in western China.

KEY WORDS: Poor compliance; Poor survival; Rectal cancer; West China; Younger onset.

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