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EDITORIAL

Radical radiotherapy without surgical tumor resection for rectal cancer

Takashi Ono, Masashi Koto

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Abstract

In this editorial, I would like to comment on the article, recently published in the *World Journal of Clinical Oncology*. The article focuses on non-surgical treatments for locally recurrent rectal cancer, including the watch-and-wait (WW) strategy after total neoadjuvant therapy (TNT) and particle beam therapy. As treatment options for rectal cancer continue to evolve, the high complete response rate achieved with TNT has led to the development of a new non-surgical approach: WW. Chemoradiotherapy followed by consolidation chemotherapy, in particular, has a low rate of tumor growth and is a treatment aimed at achieving a cure without surgery. However, the risk of recurrence within two years is significant, necessitating careful follow-up. Establishing standardized follow-up methods that can be implemented by many physicians is essential. Carbon ion radiotherapy has demonstrated high local control with a low incidence of severe late toxicities, even after previous pelvic radiotherapy. While these new non-surgical curative treatments for rectal cancer require further investigation, future advancements in this field are anticipated.

Key Words: Rectal cancer; Locally recurrent rectal cancer; Total neoadjuvant therapy; Watch-and-wait; Carbon ion radiotherapy; Proton beam therapy

Core Tip: This editorial focuses on non-surgical radical treatments for rectal cancer. Total neoadjuvant therapy has demonstrated a high complete response. This success has made the watch-and-wait strategy a viable option for some patients. However, establishing standardized follow-up methods is essential. Carbon ion radiotherapy has demonstrated high local control with a low incidence of severe late toxicities, even after previous pelvic radiotherapy. While these new non-surgical curative treatments for rectal cancer require further investigation, future advancements in this field are anticipated.

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INTRODUCTION

Colorectal cancer is a significant global health concern, accounting for one in ten cancer cases and deaths. In 2022 alone, an estimated 729702 new cases of rectal cancer and 343761 deaths were reported[1]. While screening tests can detect some cases early, many individuals with rectal cancer experience few specific symptoms and are diagnosed only after the disease has progressed.

The new standard treatment of locally advanced rectal cancer is total neoadjuvant therapy (TNT) which include neoadjuvant radiotherapy and consolidative chemotherapy[2]. For radiotherapy, the American Society for Radiation Oncology's clinical guidelines recommend either conventionally fractionated concurrent chemoradiotherapy (CRT) or short-course radiotherapy without concurrent chemotherapy. The guidelines also specify that only concurrent 5-fluorouracil or capecitabine is recommended with radiotherapy for radiosensitization[3]. Due to the intensive nature of TNT, locoregional recurrence after surgery is typically less than 10%[2].

As highlighted by Fadlallah *et al*[4], recent advancements in treatment have made it possible to pursue a cure through non-surgical approaches such as the watch-and-wait (WW) strategy and radiotherapy after local recurrence.

This editorial focuses on the potential role of radical radiotherapy without surgery as a treatment option for rectal cancer.

WW STRATEGY AFTER CRT FOR RECTAL CANCER

The WW strategy has long been considered a potential approach to preserve organs without surgery[5,6]. Recently, the Osseointegrated Prostheses for the Rehabilitation of Amputees (OPRA) trial provided the largest prospective cohort and the longest follow-up for patients with locally advanced rectal cancer undergoing WW surveillance after TNT. Although further studies are warranted, the OPRA trial showed that it is possible to cure rectal cancer without surgery, even over the long term. In this trial, more than 70% of patients were offered WW, and approximately two-thirds of those with a clinical complete response or near-complete response after TNT did not experience tumor regrowth. For cases where tumor growth after WW did occur, 94% were observed within two years, and 99% within three years[7]. A report based on large-scale registry data also showed that nearly 90% of tumor regrowth occurred within two years[6].

In the OPRA trial, patients in the CRT followed by consolidation chemotherapy (CRT-CNCT) group had a lower regrowth rate (29%) compared to the induction chemotherapy followed by CRT (INCT-CRT) group (44%). However, disease-free survival, distant metastasis-free survival, and overall survival (OS) were not significantly different between the two groups[7]. Therefore, CRT-CNCT may be a more suitable approach for WW than INCT-CRT. Nevertheless, careful consideration is needed to determine the appropriateness of this strategy, even with promising long-term results, as a certain degree of tumor regrowth will occur.

The Dutch Watch-and-Wait Consortium reported that some patients experienced bowel and sexual dysfunction, leading to a decline in quality of life and functional outcomes when subsequent surgery was required[8]. It is crucial to establish appropriate follow-up methods that minimize inconvenience for patients choosing WW and can be easily implemented by many physicians.

PARTICLE BEAM THERAPY FOR RECTAL CANCER

Despite advancements in treatment, recurrence remains a significant challenge for patients with rectal cancer, occurring in less than 10% of cases[2]. Radical surgery is an option for fewer than one-third of patients with local recurrence, and only about half of these cases achieve curative surgery. In this report, the five-year OS rate for patients undergoing curative surgery was 43%, while it was less than 15% for those without curative surgery[9].

For locally recurrent rectal cancer, radiotherapy is a curative treatment alternative to surgery. In addition to the widely used photon radiotherapy, particle beam therapy, such as carbon ion radiotherapy (CIRT) and proton beam therapy (PBT), is also available. Numerous studies have been published on CIRT. Shinoto *et al*[10] reported on a large population

of 224 cases in Japan, finding a five-year OS rate of 51% and a locoregional control (LC) rate of 88% with a median follow-up of 62 months. Importantly, this study observed less than 1% of grade 3 late gastrointestinal toxicities, with no grade 4 or grade 5 toxicities[10].

Yamada *et al*[11] reported on patients who received CIRT for locally recurrent rectal cancer after previous pelvic irradiation, finding a five-year OS rate of 38% and an LC rate of 62%. However, late infections occurred in 17% of cases, although there were no grade 4 or grade 5 toxicities. As TNT becomes the standard, more patients with previous pelvic irradiation will likely be treated; however, caution is required as toxicity will inevitably be higher and treatment less effective compared to cases without previous pelvic irradiation.

Several studies have compared particle beam therapy with photon therapy, and both have shown superior outcomes to photon radiotherapy[12,13]. These differences may be attributed to the unique characteristics of particle beam therapy, known as the Bragg peak. Particle beam therapy makes it possible to irradiate with a dose that drops sharply at the ends of the beam, making it possible to reduce irradiation of unnecessary areas compared to photon beams[14].

PBT also possesses these characteristics and is expected to be effective, but there have been fewer published studies on it compared to CIRT[15,16].

While CIRT and PBT are effective treatments, they may not be suitable for patients with bowel infiltration due to the risk of bowel perforation after treatment. To address this issue, Nagata *et al*[17] reported on prophylactic resection of the normal bowel that was irradiated eight weeks after CIRT. This approach is one possible solution to expand the therapeutic application of particle beam therapy, but further research is needed.

CONCLUSION

Given the advancements in rectal cancer treatment, non-surgical options are now available. Further research is necessary to fully understand the benefits and limitations of these new approaches.

FOOTNOTES

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