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A commentary on 'Comparison of the efficacy of neoadjuvant chemotherapy and neoadjuvant chemoradiotherapy in locally advanced rectal cancer patients: meta-analysis of randomized controlled trials'

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Preoperative neoadjuvant chemoradiotherapy (nCRT) has been considered the standard treatment strategy for locally advanced rectal cancer (LARC) for nearly two decades. Although nCRT reduced the 5-year local recurrence rate (6% vs. 13%; P = 0.006), it did not improve the distant metastasis rate and overall survival when compared with postoperative adjuvant therapy[1]. This may be because neoadjuvant radiotherapy delays the initiation of systemic therapy. Preoperative Pelvic radiotherapy also results in various short- and long-term complications, such as sphincter and bowel function.

Therefore, the role of neoadjuvant chemotherapy (nCT) alone in LARC has been explored, and it seems that nCT may result in an acceptable tumor response and long-term survival, while other studies have reported different results. Zeng *et al* conducted meta-analysis of randomized controlled trials (FOWARC, PROSPECT, GRECCAR 4 and CONVERT) to compare the efficacy of nCT and nCRT in locally advanced rectal cancer. This indicated that overall survival and disease-free survival were not lower in the nCT group than in the nCRT group, and the nCT group had fewer complications[2].

The results of this meta-analysis are encouraging, but we believe that they should be interpreted with caution. First, local recurrence rate is an important index for evaluating neoadjuvant radiotherapy. Although relevant data have been reported in PROSPECT and FOWARC[3,4], they were not used in the meta-analysis. Second, in conducting the meta-analysis of survival analyses, Zeng *et al* used data from PROSPECT and FOWARC. However, the designs of the two studies were different. PROSEPECT uses selective radiotherapy, and preoperative radiotherapy is administered to patients with inadequate tumor response. In the FOLFOX group, up to 53 patients (9.1%) in the PROSPECT trial received preoperative radiotherapy but were included in the survival analysis[3]. In addition, the long-term survival results of CONVERT have been presented in conference abstracts and the noninferiority of nCT has not been confirmed[5]. However, the study did not include data from conference abstracts, which may have led to a publication bias. At the same time, owing to the small number of included studies, the funnel plot should not be used to assess whether there was publication bias. Finally, the study did not adequately compare the population stage characteristics of these randomized, controlled trials, and we believe that the treatment of LARC should be adjusted according to risk stratification[6].

In conclusion, although nCT has great potential for the treatment of LARC, it is not simple to conclude that nCT is noninferior to nCRT. We suggest that future studies should consider the stratification of recurrence risk to design different neoadjuvant treatment strategies to identify the population subgroups suitable for neoadjuvant chemotherapy alone and ensure that patient interests are not jeopardized in clinical research.

Ethical approval

Not applicable to this study.

Consent

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Author contributions

W.Z.: study design and writing; J.D. and M.Z.: critical review; Y.W.: study supervision.

Conflicts of interest disclosure

The author declares no conflict of interest.

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References

[1] Sauer R, Becker H, Hohenberger W, *et al*. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med 2004; 351:1731–40.
[2] Zeng DX, Liu RN, Ren XK, *et al*. Comparison of the efficacy of neoadjuvant chemotherapy and neoadjuvant chemoradiotherapy in locally advanced rectal cancer patients: meta-analysis of randomized controlled trials. Int J Surg 2025;111:2686–96.
[3] Schrag D, Shi Q, Weiser MR, *et al*. Preoperative treatment of locally advanced rectal cancer. N Engl J Med 2023;389:322–34.
[4] Deng Y, Chi P, Lan P, *et al*. Neoadjuvant modified FOLFOX6 with or without radiation versus fluorouracil plus radiation for locally advanced rectal cancer: final results of the Chinese FOWARC trial. J Clin Oncol 2019;37:3223–33.
[5] Ding P, Wang X, Li Y, *et al*. LBA26 Neoadjuvant chemotherapy with CAPOX versus chemoradiation for locally advanced rectal cancer with uninvolved mesorectal fascia (CONVERT): final results of a phase III trial. Ann Oncol 2023;34:S1267–8.
[6] Glynne-Jones R, Wyrwicz L, Tiret E, *et al*. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 2017;28:v22–40.