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Is total neoadjuvant treatment beneficial for locally advanced rectal cancer? A meta-analysis of randomized controlled trials

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 July 2023 and was last updated on 31 July 2023.

INTRODUCTION

Review question / Objective To systematically evaluate the efficacy and safety of total neoadjuvant treatment (TNT) in locally advanced rectal cancer.

Condition being studied This study evaluates the efficacy and safety of total neoadjuvant therapy (TNT) compared to neoadjuvant chemoradiotherapy (CRT) for locally advanced rectal cancer, and provide high-quality evidence to guide clinical practice.

METHODS

Participant or population Patients clinically diagnosed with locally advanced rectal cancer at cT3-4 or cN+ stage.

Intervention The experimental group receives TNT combined with total mesorectal excision (TME) surgery.

Comparator The control group receives neoadjuvant CRT combined with TME surgery.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria (1) Patients clinically diagnosed with locally advanced rectal cancer at cT3-4 or cN+ stage. (2) The experimental group receives TNT combined with total mesorectal excision (TME) surgery, while the control group receives neoadjuvant CRT combined with TME surgery. (3) Published randomized controlled trials (RCTs), regardless of blinding methodology, in any language are included. (4) The outcome measures include one of the following: ① Pathologic complete response (PCR) rate. ② T0 downstaging rate. ③ R0 resection rate. ④ Sphincter preservation rate. ⑤ Anastomotic leak rate. ⑥ Grade 3 or higher adverse reactions (referring to severe or potentially life-threatening side effects).

⑦ 3-year overall survival (OS). ⑧ 3-year disease-free survival (DFS).

Information sources China National Knowledge Infrastructure, VIP Database, Wanfang Database, China Biomedical Literature Database, PubMed, Embase, and The Cochrane Library.

Main outcome(s) ① Pathologic complete response (PCR) rate. ② T0 downstaging rate. ③ R0 resection rate. ④ Sphincter preservation rate. ⑤ Anastomotic leak rate. ⑥ Grade 3 or higher adverse reactions (referring to severe or potentially life-threatening side effects). ⑦ 3-year overall survival (OS). ⑧ 3-year disease-free survival (DFS).

Quality assessment / Risk of bias analysis The quality of the included randomized controlled trials was assessed using the Cochrane Risk of Bias Assessment Tool 5.3.0. The assessment primarily included the generation of random sequences, allocation concealment, blinding of participants and personnel, blinding of outcome assessors, incomplete outcome data, selective reporting, and other biases. Each criterion was classified as low risk, unclear, or high risk. Two researchers independently conducted the assessment based on the aforementioned criteria, and in case of any discrepancies, a third researcher made the final judgment.

Strategy of data synthesis Meta-analysis was conducted using Revman 5.3 software. For dichotomous variables, the risk ratio (RR) and 95% confidence interval (CI) were used as statistical measures. The inverse variance method was employed for statistical analysis of survival data for overall survival (OS) and disease-free survival (DFS), using the hazard ratio (HR) and 95% CI as statistical measures. Heterogeneity of included studies was assessed qualitatively using the Q-test and I2-test. When there was no significant heterogeneity among the included study results ($P>0.1$, $I2<50\%$), a fixed-effects model was used to combine the results. In cases where there was significant heterogeneity among the study results ($P<0.1$, $I2>50\%$), subgroup analysis was performed based on factors that could potentially cause heterogeneity. If there was no significant heterogeneity within subgroups, a random-effects model was used for the combined analysis; otherwise, a descriptive evaluation was conducted. If the source of heterogeneity remained unclear, a random-effects model was used for the combined analysis of all included study results. Sensitivity analysis was performed to evaluate the stability of the results. Funnel plots and Egger's test were used for publication bias analysis for indicators with more than 10 included studies. $P<0.05$ indicates a statistically significant difference.

Subgroup analysis Subgroup analysis was conducted for studies with obvious heterogeneity.

Sensitivity analysis Sensitivity analysis was repeated each time after a single study was removed to evaluate the impact of the study on the combined effect and evaluate the impact of the study on this indicator.

Country(ies) involved China.

Keywords rectal cancer; neoadjuvant radiochemotherapy; surgery; meta-analysis.

Contributions of each author
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Author 3 - Ji-Dong Miao.
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