

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2020 December 15; 12(12): 1381-1463



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ABOUT COVER

Editorial Board Member of *World Journal of Gastrointestinal Oncology*, Dr. Lin is a distinguished professor at the Hebei Medical University in Shijiazhuang, China. Dr. Lin received his Bachelor's degree from Tianjin Medical University in 1998 and undertook his postgraduate training at Hebei Medical University, receiving his PhD in 2007. He rose to Chief Oncologist in the Department of Oncology, North China Petroleum Bureau General Hospital Affiliated to Hebei Medical University in 2013 and has held the position since. Further, he has served as one of the academic leaders of the five Key Developing Disciplines (Oncology) in Hebei Province since 2017. He also currently serves as Secretary General of the Clinical Committee of Anticancer Drugs, China Pharmaceutical Industry Research and Development Association. His ongoing research interests involve the application of evidence-based medicine in digestive oncology and thoracic oncology. (L-Editor: Filipodia)

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WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

INDEXING/ABSTRACTING

The *WJGO* is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, and PubMed Central. The 2020 edition of Journal Citation Reports® cites the 2019 impact factor (IF) for *WJGO* as 2.898; IF without journal self cites: 2.880; 5-year IF: 3.316; Ranking: 143 among 244 journals in oncology; Quartile category: Q3; Ranking: 55 among 88 journals in gastroenterology and hepatology; and Quartile category: Q3.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Jia-Hui Li; Production Department Director: Xiang Li; Editorial Office Director: Jin-Lei Wang.

NAME OF JOURNAL

World Journal of Gastrointestinal Oncology

ISSN

ISSN 1948-5204 (online)

LAUNCH DATE

February 15, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Rosa M Jimenez Rodriguez, Pashtoon Kasi, Monjur Ahmed

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-5204/editorialboard.htm>

PUBLICATION DATE

December 15, 2020

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<https://www.wjgnet.com/bpg/gerinfo/208>

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<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Prognostic impact of at least 12 lymph nodes after neoadjuvant therapy in rectal cancer: A meta-analysis

Ling Tan, Zi-Lin Liu, Zhou Ma, Zhou He, Lin-Han Tang, Yi-Lei Liu, Jiang-Wei Xiao

ORCID number: Ling Tan 0000-0001-5442-5184; Zi-Lin Liu 0000-0003-0113-9912; Zhou Ma 0000-0002-0991-2386; Zhou He 0000-0002-4811-9911; Lin-Han Tang 0000-0003-1918-1262; Yi-Lei Liu 0000-0001-9108-8113; Jiang-Wei Xiao 0000-0002-4288-7581.

Author contributions: Tan L and Liu ZL performed data acquisition, analysis, and interpretation, and drafted the manuscript; Ma Z, He Z, Tang LH, and Liu YL contributed to data interpretation and revised the manuscript; Xiao JW contributed to study conception and design, and critical revision of the manuscript; all authors approved the final version of the submitted manuscript.

Supported by the National Natural Science Foundation of China, No. 81070378 and 81270561; and Special Research Fund for The First Affiliated Hospital of Chengdu Medical College, No. CYFY2019YB08.

Conflict-of-interest statement: All the authors declare that they have no conflict of interest to disclose.

PRISMA 2009 Checklist statement: The authors have read the PRISMA 2009 Checklist, and the manuscript was prepared and revised according to the PRISMA 2009 Checklist.

Ling Tan, Zi-Lin Liu, Zhou Ma, Zhou He, Lin-Han Tang, Yi-Lei Liu, Jiang-Wei Xiao, Department of Gastrointestinal Surgery, Clinical Medical College and The First Affiliated Hospital of Chengdu Medical College, Chengdu 610500, Sichuan Province, China

Corresponding author: Jiang-Wei Xiao, MD, PhD, Postdoc, Professor, Surgeon, Surgical Oncologist, Teacher, Department of Gastrointestinal Surgery, Clinical Medical College and The First Affiliated Hospital of Chengdu Medical College, No. 278 Zhongduan Baoguang Avenue, Xindu District, Chengdu 610500, Sichuan Province, China. xiaojiangwei2018@163.com

Abstract

BACKGROUND

The number of dissected lymph nodes (LNs) in rectal cancer after neoadjuvant therapy has a controversial effect on the prognosis.

AIM

To investigate the prognostic impact of the number of LN dissected in rectal cancer patients after neoadjuvant therapy.

METHODS

We performed a systematic review and searched PubMed, Embase (Ovid), MEDLINE (Ovid), Web of Science, and Cochrane Library from January 1, 2000 until January 1, 2020. Two reviewers examined all the publications independently and extracted the relevant data. Articles were eligible for inclusion if they compared the number of LNs in rectal cancer specimens resected after neoadjuvant treatment (LNs ≥ 12 vs LNs < 12). The primary endpoints were the overall survival (OS) and disease-free survival (DFS).

RESULTS

Nine articles were included in the meta-analyses. Statistical analysis revealed a statistically significant difference in OS [hazard ratio (HR) = 0.76, 95% confidence interval (CI): 0.66-0.88, $I^2 = 12.2\%$, $P = 0.336$], DFS (HR = 0.76, 95% CI: 0.63-0.92, $I^2 = 68.4\%$, $P = 0.013$), and distant recurrence (DR) (HR = 0.63, 95% CI: 0.48-0.93, $I^2 = 30.5\%$, $P = 0.237$) between the LNs ≥ 12 and LNs < 12 groups, but local recurrence (HR = 0.67, 95% CI: 0.38-1.16, $I^2 = 0\%$, $P = 0.348$) showed no statistical difference. Moreover, subgroup analysis of LN negative patients revealed a statistically significant difference in DFS (HR = 0.67, 95% CI: 0.52-0.88, $I^2 = 0\%$, $P = 0.565$) between the LNs ≥ 12 and LNs < 12 groups.

CONCLUSION

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Manuscript source: Unsolicited manuscript

Specialty type: Oncology

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
 Grade B (Very good): B, B
 Grade C (Good): C
 Grade D (Fair): 0
 Grade E (Poor): 0

Received: August 5, 2020

Peer-review started: August 5, 2020

First decision: September 24, 2020

Revised: September 28, 2020

Accepted: October 20, 2020

Article in press: October 20, 2020

Published online: December 15, 2020

P-Reviewer: Grundmann R, Uhlmann D

S-Editor: Chen XF

L-Editor: Wang TQ

P-Editor: Li JH



Although neoadjuvant therapy reduces LN production in rectal cancer, our data indicate that dissecting at least 12 LNs after neoadjuvant therapy may improve the patients' OS, DFS, and DR.

Key Words: Rectal cancer; Neoadjuvant therapy; Lymph node; Prognostic; Overall survival; Meta-analysis

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Core Tip: After neoadjuvant treatment of rectal cancer, the lymph node (LN) output is significantly reduced. There is no consensus on the relationship between the number of LNs resected and the prognosis of rectal cancer after neoadjuvant treatment. This is the first meta-analysis to compare the impact of the number of LNs on the prognosis of rectal cancer after neoadjuvant treatment. We studied the effects of resection of at least 12 LNs and less than 12 LNs after neoadjuvant treatment of rectal cancer on overall survival, disease-free survival, distant recurrence, and local recurrence.

Citation: Tan L, Liu ZL, Ma Z, He Z, Tang LH, Liu YL, Xiao JW. Prognostic impact of at least 12 lymph nodes after neoadjuvant therapy in rectal cancer: A meta-analysis. *World J Gastrointest Oncol* 2020; 12(12): 1443-1455

URL: <https://www.wjgnet.com/1948-5204/full/v12/i12/1443.htm>

DOI: <https://dx.doi.org/10.4251/wjgo.v12.i12.1443>

INTRODUCTION

Colorectal cancer is ranked third and second among global cancer morbidity and mortality, respectively. The incidence rate of colorectal cancer is third in men and fourth in women^[1]. In 2018, 43030 new cases of rectal cancer were diagnosed in the United States^[2].

According to both the International Union Against Cancer (UICC) and American Joint Commission on Cancer (AJCC), a minimum of 12 lymph nodes (LNs) should be obtained from surgical specimens to stage a colorectal cancer^[3,4]. Today, the standard of care for patients with locally advanced rectal cancer is neoadjuvant chemoradiation therapy (CRT), followed by total mesorectal excision (TME)^[5,6]. However, many studies have reported a significant decrease in the number of LNs retrieved from patients with rectal cancer who have received preoperative chemoradiation^[7-12]. For example, a meta-analysis reported an average reduction of 3.9 LNs in neoadjuvant CRT compared with no neoadjuvant CRT^[12]. Therefore, it remains controversial whether 12 or more resected LNs should be recommended by the UICC or AJCC after many neoadjuvant treatments for rectal cancer.

In the past 20 years, neoadjuvant therapy has been widely applied in rectal cancer. An increasing number of scholars have focused on the influence of the number of resected LNs after neoadjuvant therapy on the prognosis of rectal cancer. Presently, resecting more than 12 LNs or fewer than 12 LNs after neoadjuvant treatment for rectal cancer is controversial for prognosis.

Given the prognostic impact of the number of LNs, we performed a first series of meta-analyses to compare the prognostic impact of surgical resection of greater than 12 vs fewer than 12 LNs in patients with rectal cancer after neoadjuvant treatment.

MATERIALS AND METHODS

Search strategy and inclusion criteria

For this systematic review, we adhered to the Meta-analysis of Observational Studies guidelines^[13] and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis statement^[14]. A systematic search was performed based on the following databases: PubMed, Embase (Ovid), MEDLINE (Ovid), Web of Science, and Cochrane Library from January 1, 2000 to January 1, 2020. We used "rectal cancer", "neoadjuvant

therapy”, “preoperative radiotherapy”, “preoperative chemotherapy”, “lymph nodes” and corresponding free words to search the literature in the above databases. Regardless of the type of study, the articles were eligible for inclusion if they compared the number of LNs in rectal cancer specimens resected after neoadjuvant treatment (LNs \geq 12 *vs* LNs $<$ 12).

First, all the identified titles and abstracts were examined by two independent reviewers (Tan L and Liu ZL). Next, the same two reviewers independently examined the full text of potentially relevant articles. In the event of disagreement, a third reviewer (Ma Z) was consulted and the relevant articles were discussed until a consensus was reached.

Data extraction and quality assessment

The following relevant information was extracted from all the included publications: First author, year of publication, country, number of patients, age, tumor grade, neoadjuvant therapy, surgery, years of follow-up, and outcome type. The main outcomes were the overall survival (OS) and disease-free survival (DFS) differences between the LNs \geq 12 and LNs $<$ 12 groups in patients after neoadjuvant therapy. The secondary outcomes were the distant recurrence (DR) and local recurrence (LR) differences between the LNs \geq 12 and LNs $<$ 12 groups in patients after neoadjuvant therapy. Therefore, if available, the following data were extracted: Hazard ratios (HRs), 95% confidence intervals (CIs), and *P* values of OS, DFS, DR, and LR. When the literature did not report HRs, only OS and DFS Kaplan-Meier curves and Engauge Digitizer (version 10.8) were used to determine the survival rate at the corresponding time points on the curve, followed by the HR calculation table^[15]. We took the countdown if the HR reported in the literature was LNs $<$ 12 *vs* LNs \geq 12. All the data were independently extracted by two authors (Tan L and Liu ZL) and compared for consistency.

The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), with a maximum of nine points per study. Publication bias was assessed by visual inspection of the symmetry of the funnel plot. Since we considered that DFS heterogeneity was derived from patients with positive LNs, we performed subgroup analysis of the DFS of LN negative patients based on LNs \geq 12 *vs* LNs $<$ 12.

Statistical analysis

We used the Stata (version 15.3) Meta package for meta-analysis^[16]. Binary outcome data are reported as HRs with 95% CIs using the Mantel-Haenszel method. Weighted mean differences were calculated for the effect size of continuous variables. Heterogeneity was assessed using *I*² statistics, with values above 50% considered considerable heterogeneity. An *a priori* decision to use the random-effects model was made to account for the assumed considerable heterogeneity between the studies.

RESULTS

After removing duplicates, our computer-aided search yielded 11871 publications from PubMed, Medline (Ovid), Embase (Ovid), Web of Science, and Cochrane Library (Figure 1). In total, nine publications and 4494 patients with rectal cancer were eligible for inclusion. Table 1 indicates the characteristics of the included studies. Seven^[17-23] of the nine studies (3840 patients) reported the main endpoint of OS; five^[17,19-21,24] of the nine studies (1811 patients) reported the endpoint of DFS; three^[17,23,25] of nine studies (953 patients) reported the endpoint of DR; two^[17,25] of the nine studies (716 patients) reported the endpoint of LR. The NOS scores of the nine studies ranged from eight to nine (Figure 2). The literature collected was considered to be qualified.

Primary endpoints

OS for LNs \geq 12 *vs* LNs $<$ 12: Seven of the nine included studies reported OS data based on at least 12 LNs *vs* fewer than 12 LNs; the HRs and 95% CIs of these studies and the summary HRs are shown in Figure 3A. The total summary estimated HR was 0.76 (95% CI: 0.66-0.88, *P* = 0.336). Heterogeneity tests showed that the trials did not have heterogeneity (*I*² = 12.2%, *P* = 0.336).

DFS for LNs \geq 12 *vs* LNs $<$ 12: Among the nine studies collected, five reported DFS data based on at least 12 LNs and fewer than 12 LNs; the 95% CIs and HRs for each study and the summary HRs are shown in Figure 3B. The total summary estimated HR was 0.76 (95% CI: 0.63-0.92, *P* = 0.013). Heterogeneity tests showed that the trials had

Table 1 Characteristics of studies included in the meta-analysis

Ref.	Country	n	Age (yr)	Stage	Treatment	Surgery	Year of follow-up	Outcome
Wang <i>et al</i> ^[17] , 2019	China	495	< 50: 160; > 50: 335	I-IV	Neoadjuvant treatment (RT 45-55 Gy + capecitabine)	AR, APR, Hartmann	No report	OS, DFS, LR, DR
Lykke <i>et al</i> ^[18] , 2015	Denmark	2123	60-75	I-IV	Neoadjuvant treatment	TME	No report	OS
de Campos-Lobato <i>et al</i> ^[23] , 2013	United States	237	57 (49-66)	II-III	Neoadjuvant treatment	LAR, APR	55 (36-77) mo	OS, DR, LR
Kim <i>et al</i> ^[20] , 2015	South Korea	302	39-73	I-IV	Neoadjuvant treatment (IV 5-FU leucovorin or oral 5-FU based)	LAR, APR, CAA	57 mo	OS, DFS
Doll <i>et al</i> ^[22] , 2009	Germany	102	18-75	I-IV	Neoadjuvant di chemotherapy (RT 45 Gy + 5-FU)	(L)AR, Miles	No reports	OS
La Torre <i>et al</i> ^[19] , 2013	Italy	123	67.9 (27-91)	I-IV	Neoadjuvant di chemotherapy (RT 45 Gy + 5-FU)	LAR, APR	50 (9-120) mo	OS, DFS
Kim <i>et al</i> ^[24] , 2015	South Korea	433	62 ± 11.1	I-IV	Perioperative chemoradiation (45.0-50.4 Gy + 5-FU and leucovorin)	TME	41.2 mo	DFS
Han <i>et al</i> ^[21] , 2016	South Korea	458	60 (22-99)	I-III	Neoadjuvant treatment (RT 45-50.4 Gy + 5-FU)	TME	52 mo	OS, DFS
Klos <i>et al</i> ^[25] , 2010	United States	221	53 ± 13	-	neoadjuvant treatment (RT 45.0-50.4 Gy + 5-FU)	TME	36 (21.6-63.6) mo	LR, DR

OS: Overall survival; DFS: Disease-free survival; DR: Distant recurrence; LR: Local recurrence; RT: Radiotherapy; 5-FU: 5-Fluorouracil; TME: Total mesorectal excision; APR: Abdominoperineal resection; LAR: Low anterior resection; CAA: Coloanal anastomosis; AR: Anterior resection.

significant heterogeneity ($I^2 = 68.4\%$, $P = 0.013$).

Secondary endpoints

DR for LNs ≥ 12 vs LNs < 12 : Three of the nine included studies reported DR data based on LN ≥ 12 vs LN < 12 ; the 95% CIs and HRs for each study and the summary HRs are shown in [Figure 3C](#). The total summary estimated HR was 0.67 (95% CI: 0.48-0.93, $P = 0.237$). Heterogeneity tests showed that the trials had no significant heterogeneity ($I^2 = 30.5\%$, $P = 0.237$).

LR for LNs ≥ 12 vs LNs < 12 : Two of the nine included studies reported LR data based on LN ≥ 12 vs LN < 12 . The total summary estimated HR was 0.67 (95% CI: 0.38-1.16, $P = 0.348$), with no statistical significance.

Sensitivity analysis

Sensitivity analysis showed that any deletion of a set of data had no effect on the results ([Figure 4](#)). We considered heterogeneity in patients with LN positivity. So, we conducted subgroup analysis of LN negative patients; the HRs and 95% CIs for each study and the summary HRs are shown in [Figure 5](#). The total summary estimated HR was 0.67 (95% CI: 0.52-0.88), and no heterogeneity was found.

Publication bias

Publication bias was assessed by visual examination of the symmetry of the funnel plot. Our funnel plot showed no publication bias ([Figure 6](#)).

DISCUSSION

The AJCC and College of American Pathologists recommend examination of a minimum of 12 LNs to stage rectal cancer accurately. Sampling of 12 LNs may not be achievable in patients who have received neoadjuvant chemoradiation therapy^[4,26]. Therefore, it remains controversial whether 12 LNs can be used as an accurate staging index for rectal cancer patients who have received preoperative neoadjuvant

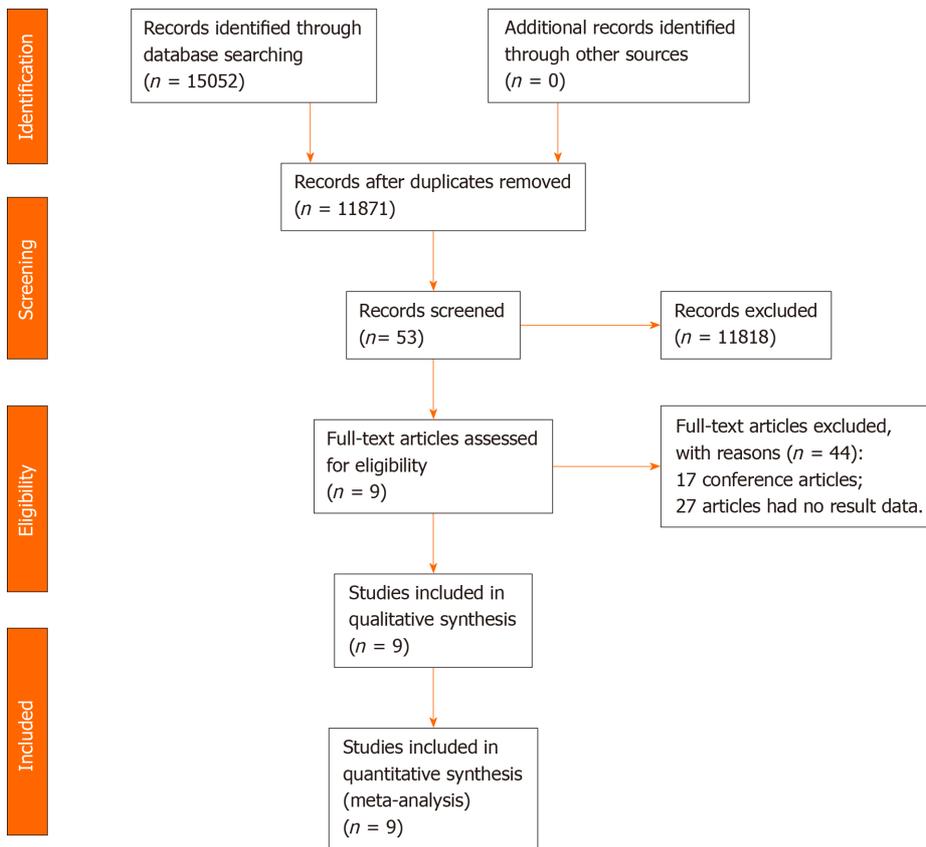


Figure 1 Flowchart of search strategy and study selection.

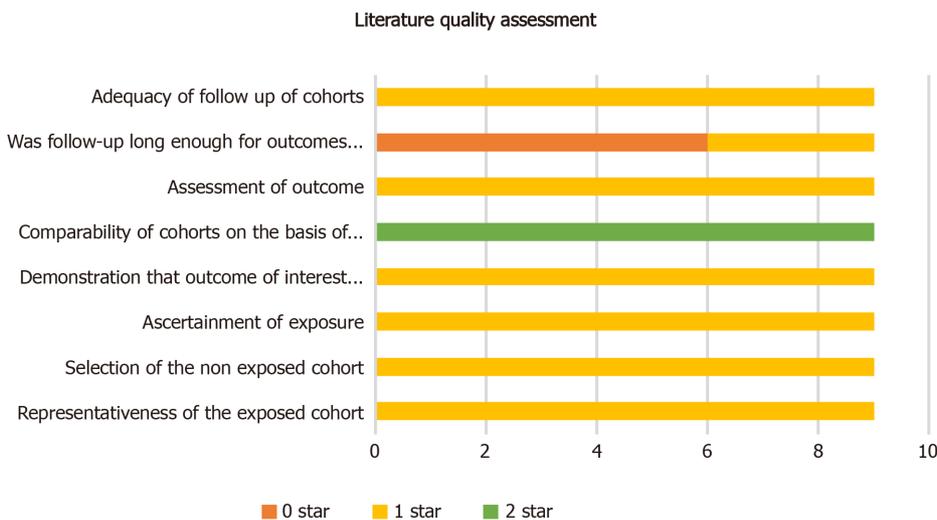


Figure 2 Literature quality assessment based on the Newcastle-Ottawa Scale.

chemoradiation therapy. The mean number of LNs retrieved from rectal cancers treated with neoadjuvant therapy is significantly lower than that from rectal cancers treated by surgery alone^[8,9]. The number of LNs needed to stage neoadjuvant-treated cases accurately is unknown. In patients receiving neoadjuvant radiotherapy and chemotherapy, the number of LN dissections needs to reach 12. Is this requirement suitable as a risk factor to evaluate the prognosis of patients with rectal tumors? Is it possible that the number of evaluated LN dissections is fewer than 12 because neoadjuvant radiotherapy and chemotherapy will lead to a decrease in the number of LN dissections? To confirm whether the number of LN dissections to judge the prognosis of rectal cancer patients who received neoadjuvant radiotherapy and chemotherapy is still applicable to 12, we performed this meta-analysis study.

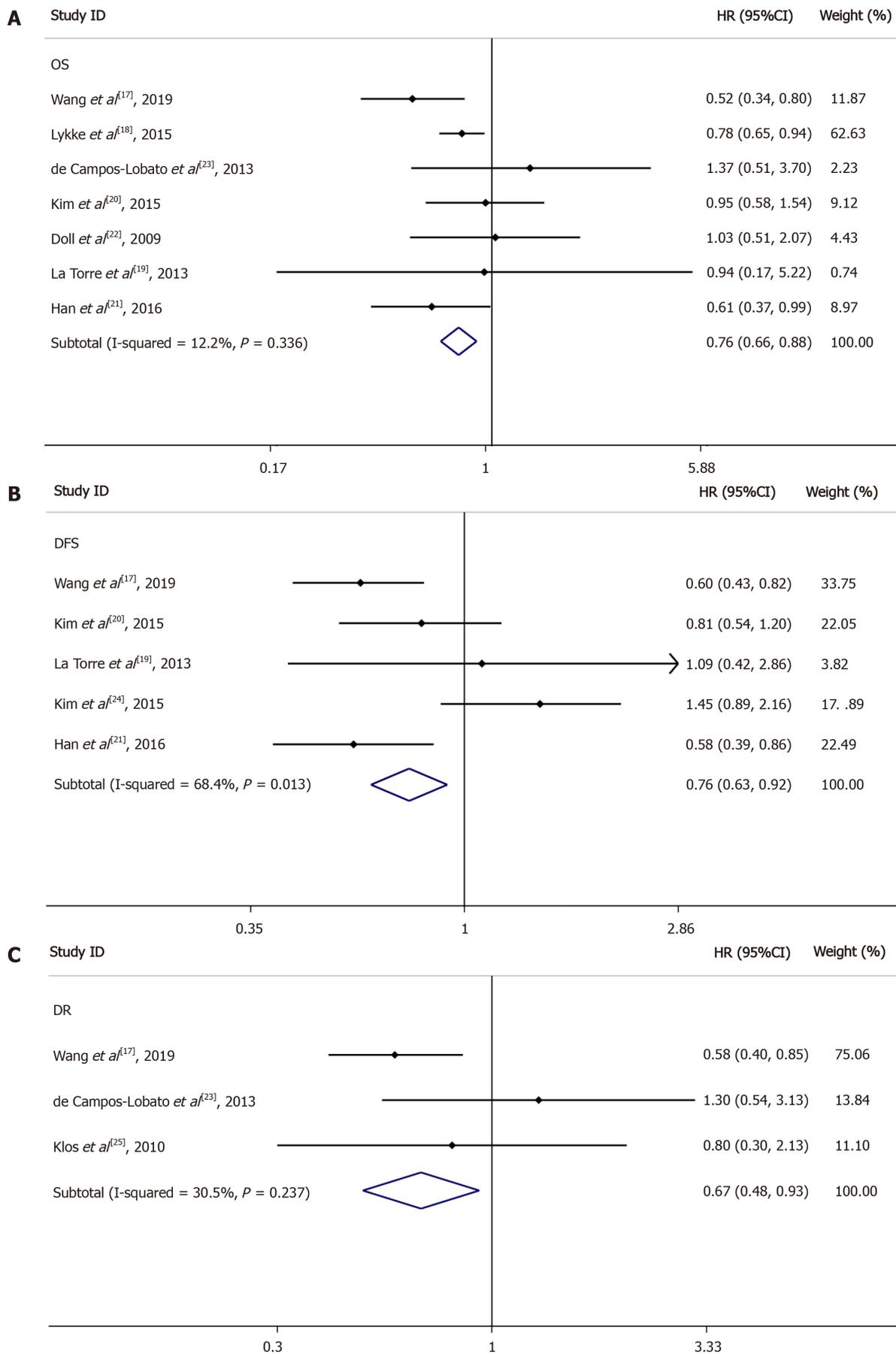


Figure 3 Forest plots for the meta-analyses. A: Overall survival; B: Disease-free survival; C: Distant recurrence. HR: Hazard ratio; CI: Confidence interval; OS: Overall survival; DFS: Disease-free survival; DR: Distant recurrence.

The main finding of the present study is that, among patients with rectal cancer, dissecting at least 12 LNs after neoadjuvant treatment improved OS and DR compared with dissecting fewer than 12 LNs. In this study, we confirmed that at least 12 LNs should be dissected in rectal cancer patients after neoadjuvant radiotherapy and chemotherapy to evaluate the prognosis of patients well, and the number of LNs dissected was closely related to the improvement in the survival rate of rectal cancer patients. Additionally, for subgroup analysis, the DFS of LN negative patients with greater than 12 LNs resected was better than that of patients with fewer than 12 LNs dissected. These data suggest that surgical resection of at least 12 LNs after neoadjuvant treatment of rectal cancer improves prognosis.

Most scholars agree that the LN yield affects the prognosis of rectal cancer. Presently, they have studied the effect of resection of 12 LNs on the prognosis. At the same time, many scholars have studied the effect of different numbers of LNs resected on the prognosis of patients with neoadjuvant therapy for rectal cancer. We summarize the literature on the effect of different LN numbers on the prognosis in the last 10 years (Table 2). Yeo *et al.*^[27] showed that at least 8.5 LNs removed from rectal cancer surgery after neoadjuvant therapy could significantly improve the 5-year OS. La Torre *et al.*^[19], Tsai *et al.*^[28], and Han *et al.*^[21] found that at least 6, 7, and 8 LNs resected after neoadjuvant treatment could improve the prognosis. Pitto *et al.*^[29] found that at least 10 to 20 LNs resected after neoadjuvant radiotherapy improved the 5-year OS compared with fewer than 9 and more than 20. The above studies indicated that the small number of LNs dissected after neoadjuvant therapy is not a sign of a good tumor response to neoadjuvant therapy, and a relatively large number of LNs is still needed to be dissected to ensure a good prognosis.

The prognostic impact of resecting more than 12 LNs and fewer than 12 LNs after neoadjuvant treatment for rectal cancer is controversial. For example, Dev *et al.*^[30] found that resecting fewer than 12 LNs in rectal cancer patients undergoing neoadjuvant radiotherapy should be considered a better prognostic factor, but Wang *et al.*^[31] and Lykke *et al.*^[18] believed that resecting at least 12 LNs is an independent and favorable prognostic factor for rectal cancer after neoadjuvant therapy. Moreover, Khan *et al.*^[32] and La Torre *et al.*^[19] believed that at least 12 LNs dissected after neoadjuvant treatment of rectal cancer do not affect the prognosis. Our meta-analysis combining the available data showed that resection of at least 12 LNs after neoadjuvant therapy improves the prognosis.

The LN harvest is influenced by several factors, including the patient's anatomic and pathologic workup, surgical dissection technique, and use of methylene blue and neoadjuvant treatment^[12,33-36]. Pathological techniques are considered a factor that affects the LN yield due to improper specimen analysis and processing. Factors associated with patients, such as advanced age and obesity, are associated with lower LN yields^[9,34,37,38]. Standard TME should be performed to help achieve optimal tumor resection. The injection of methylene blue solution into the inferior mesenteric artery is an effective and simple way to increase the LN harvest in the histopathological examination of the TME of rectal specimens^[39], especially those receiving neoadjuvant therapy^[40-42]. Presently, the use of neoadjuvant radiotherapy and chemotherapy is the standard treatment for rectal cancer in many European countries, leading to fewer LN tests^[43]. If 12 LNs are considered the number needed for the accurate staging of stage II tumors, only 20% of cases treated with neoadjuvant therapy had adequate LN sampling^[9]. To date, the number of dissected LNs needed to stage neoadjuvant-treated cases accurately is unknown. Additionally, the clinical significance of this information is unknown in the neoadjuvant setting because postoperative therapy is indicated in all patients who receive preoperative therapy regardless of the surgical pathology results. Therefore, technical measures are needed to improve the postoperative LN detection rate in patients with rectal cancer after neoadjuvant radiotherapy and chemotherapy. For example, standard TME in combination with the injection of methylene blue into the inferior mesenteric artery can be used to increase LN yield after neoadjuvant therapy. At the same time, the application of nano-carbon lymphatic tracer technology can also effectively improve the detection rate of postoperative LNs in patients with rectal cancer.

In recent decades, the therapeutic effect of rectal cancer has made great progress with the development of laparoscopic technology and medical devices. Murphy *et al.*^[44] found that the 5-year relative survival of rectal cancer improved significantly from 1992-1996 to 2010-2014. The emergence of neoadjuvant therapy, especially neoadjuvant radiotherapy and chemotherapy, significantly reduced the local recurrence rate and tumor staging of patients^[45,46]. Neoadjuvant radiotherapy and chemotherapy have been regarded as the standard treatments for locally advanced rectal cancer, and the side effects of neoadjuvant radiotherapy and chemotherapy

Table 2 Prognosis of different lymph node yield after neoadjuvant therapy for rectal cancer

Ref.	n	Treatment	Number of LNs compared	OS (HR or percent)	DFS (HR or percent)
Yeo <i>et al</i> ^[27] , 2020	94	Neoadjuvant CRT (RT 45 Gy + capecitabine)	LN _s ≥ 8.5 vs LN _s < 8.5 LN _s ≥ 16.5 vs LN _s < 16.5	HR: 0.31 (95%CI: 0.15-0.64, P < 0.001) -	- HR: 0.46 (95%CI: 0.17-1.27, P = 0.13)
La Torre <i>et al</i> ^[19] , 2013	123	Neoadjuvant CRT (RT 45 Gy + 5-FU)	LN _s ≥ 6 vs LN _s < 6	5-yr OS: 84% vs 75% (P = 0.03)	5-yr DFS: 83% vs 75% (P = 0.03)
Tsai <i>et al</i> ^[28] , 2011	372	Neoadjuvant CRT (RT 45 Gy + 5-FU and/or capecitabine)	LN _s > 7 vs LN _s ≤ 7	5-yr OS: 86.9% vs 81% (P = 0.067)	-
Han <i>et al</i> ^[21] , 2016	458	Neoadjuvant CRT (RT 45-50.4 Gy + 5-FU)	LN _s ≥ 8 vs LN _s < 8	HR: 0.5 (95%CI: 0.2-0.9, P = 0.002)	HR: 0.6 (95%CI: 0.4-1.1, P = 0.042)
Pitto <i>et al</i> ^[29] , 2020	104	Neoadjuvant RT (RT 45 Gy + capecitabine)	LN _s : 10-20 vs LN _s ≤ 9 and ≥ 20	-	HR: 0.313 (95%CI: 0.1-0.99, P = 0.049)

OS: Overall survival; DFS: Disease-free survival; LNs: Lymph nodes; HR: Hazard ratio; CRT: Chemoradiation therapy; RT: Radiotherapy; 5-FU: 5-Fuorouracil; CI: Confidence interval.

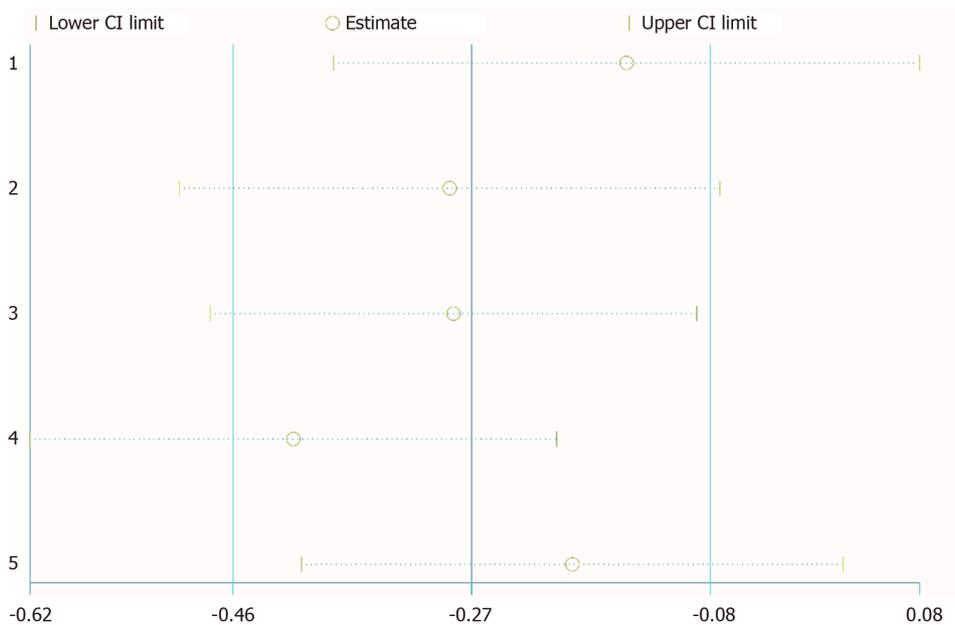


Figure 4 Sensitivity map for the meta-analysis of disease-free survival. CI: Confidence interval.

cannot be ignored, such as chronic sexual dysfunction^[47] and diarrhea^[48,49]. Some patients with high-risk diseases may need more intensive treatment, while others may have severe side effects due to the use of current protocols^[50]. The criteria for the inclusion of patients with rectal cancer to undergo neoadjuvant radiotherapy and chemotherapy need to be further optimized, and multidisciplinary team discussion is warranted to determine whether a patient should receive neoadjuvant therapy for rectal cancer.

This meta-analysis was mostly limited by its inclusion of cohort study data only; no randomized controlled study was included. Cohort studies are prone to introduce bias, and two of these studies did have OS results. The HR data in four studies could not be extracted directly and were calculated from Kaplan-Meier curves, a calculation process that may cause errors. Additionally, this study only analyzed the prognosis of patients in the LN_s ≥ 12 and LN_s < 12 groups after neoadjuvant therapy. Insufficient data existed to analyze the effect of other LN numbers on the prognosis. Differences in surgical treatment reported in the literature, as well as different surgical procedures, may influence the LN yield, which may lead to bias.

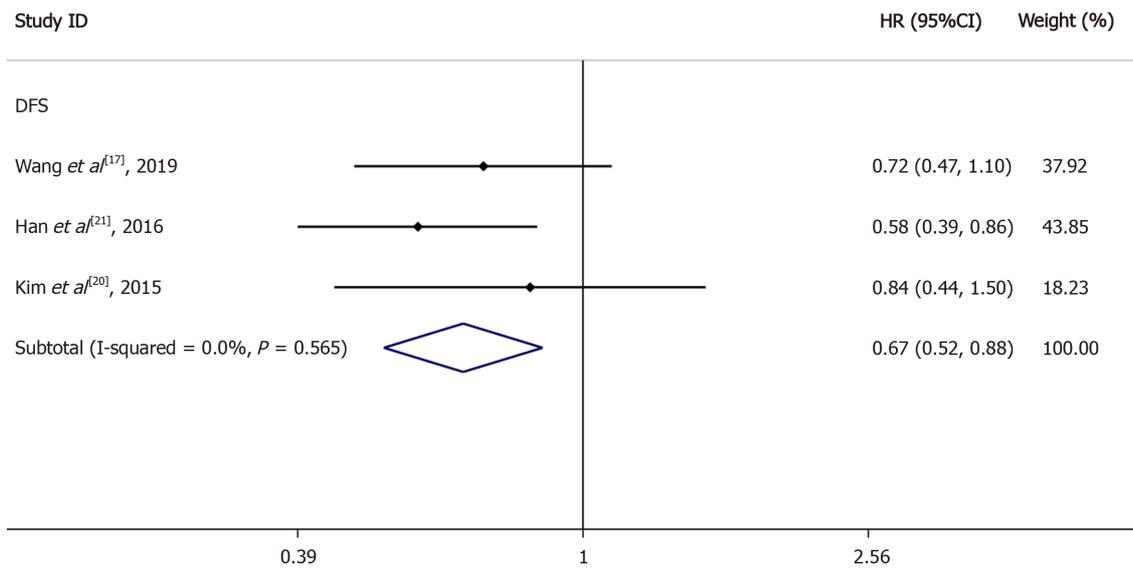


Figure 5 Forest plot for the meta-analysis of disease-free survival in the subgroup of lymph node negative patients. HR: Hazard ratio; CI: Confidence interval; DFS: Disease-free survival.

CONCLUSION

Although neoadjuvant therapy reduces the production of LNs in rectal cancer, our data indicate that dissecting at least 12 LNs after neoadjuvant therapy may improve the patients' OS, DFS, and DR.

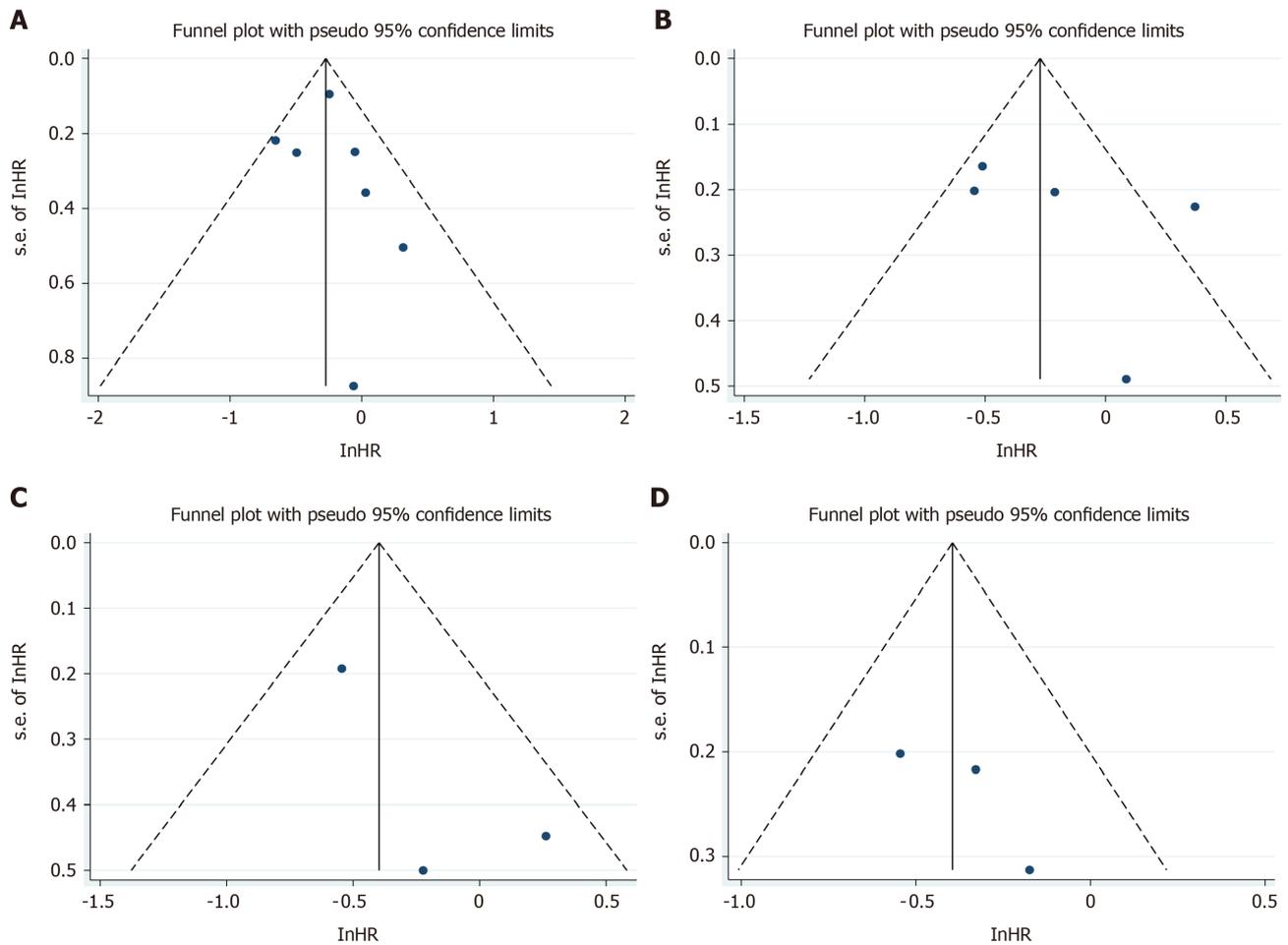


Figure 6 Funnel plot of publication bias in the meta-analysis. A: Overall survival; B: Disease-free survival; C: Distant recurrence; D: Disease-free survival in lymph node negative patients. HR: Hazard ratio.

ARTICLE HIGHLIGHTS

Research background

Neoadjuvant therapy significantly reduces the number of yielded lymph nodes (LNs) for rectal cancer, and the number of dissected LNs in rectal cancer after neoadjuvant therapy has a controversial effect on the prognosis.

Research motivation

Studies have shown that the number of LNs after rectal cancer is significantly reduced after neoadjuvant therapy. Some scholars have found that less than 12 LNs in rectal cancer patients receiving neoadjuvant radiotherapy should be considered as a better prognostic factor. However, others believe that dissecting at least 12 LNs is an independent and favorable prognostic factors for rectal cancer after neoadjuvant therapy. Therefore, it is necessary to conduct a meta-analysis to systematically and comprehensively study the influence of the number of LNs retrieved after neoadjuvant treatment on the survival outcome of patients with rectal cancer.

Research objectives

To evaluate the effect of LN production in rectal cancer after neoadjuvant treatment on survival through meta-analysis.

Research methods

The meta-analysis methods were adopted to realize the objectives.

Research results

Nine articles were included in the meta-analyses. Statistical analysis revealed a statistically significant difference in overall survival (OS) [hazard ratio (HR) = 0.76,

95% confidence interval (CI) = 0.66-0.88, $I^2 = 12.2\%$, $P = 0.336$], disease-free survival (DFS) (HR = 0.76, 95%CI: 0.63-0.92, $I^2 = 68.4\%$, $P = 0.013$), and distant recurrence (DR) (HR = 0.63, 95%CI: 0.48-0.93, $I^2 = 30.5\%$, $P = 0.237$) between the LNs ≥ 12 and LNs < 12 groups, but local recurrence (HR = 0.67, 95%CI: 0.38-1.16, $I^2 = 0\%$, $P = 0.348$) showed no statistical difference. Moreover, subgroup analysis of LN negative patients revealed a statistically significant difference in DFS (HR = 0.67, 95%CI: 0.52-0.88, $I^2 = 0\%$, $P = 0.565$) between the LNs ≥ 12 and LNs < 12 groups.

Research conclusions

This meta-analysis confirmed that dissecting at least 12 LNs after neoadjuvant therapy may improve the patients' OS, DFS, and DR.

Research perspectives

Some limitations in this analysis should be handled carefully. The most important limitation is that the included studies are all retrospective. Because some potential deviations are difficult to adjust, further careful design and large-scale randomized controlled trial experiments are needed to determine the effect of the number of anatomical LNs on the prognosis of rectal cancer after neoadjuvant treatment. In addition, because neoadjuvant therapy reduces LN yield, further research is needed on the impact of different LN numbers on prognosis, such as 6 LNs, 7 LNs, and 8 LNs.

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