Log odds of positive lymph nodes as a novel prognostic predictor for colorectal cancer: a systematic review and meta-analysis

Yiding Li1†, Guiling Wu2†, Yujie Zhang3, Ben Han4, Wanli Yang1, Xiaqian Wang1, Lili Duan1, Liaoran Niu1, Junfeng Chen1, Wei Zhou1, Jinqiang Liu1, Daiming Fan1 and Liu Hong1*

Abstract
Background: Colorectal cancer (CRC) is the third most prevalent cancer in the world, which remains one of the leading causes of cancer-related deaths. Accurate prognosis prediction of CRC is pivotal to reduce the mortality and disease burden. Lymph node (LN) metastasis is one of the most commonly used criteria to predict prognosis in CRC patients. However, inaccurate surgical dissection and pathological evaluation may lead to inaccurate nodal staging, affecting the effectiveness of pathological N (pN) classification in survival prediction among patients with CRC. In this meta-analysis, we aimed to estimate the prognostic value of the log odds of positive lymph nodes (LODDS) in patients with CRC.

Methods: PubMed, Medline, Embase, Web of Science and the Cochrane Library were systematically searched for relevant studies from inception to July 3, 2021. Statistical analyses were performed on Stata statistical software Version 16.0 software. To statistically assess the prognostic effects of LODDS, we extracted the hazard ratio (HR) and 95% confidence interval (CI) of overall survival (OS) and disease-free survival (DFS) from the included studies.

Results: Ten eligible articles published in English involving 3523 cases were analyzed in this study. The results showed that LODDS1 and LODDS2 in CRC patients was correlated with poor OS compared with LODDS0 (LODDS1 vs. LODDS0: HR = 1.77, 95% CI (1.38, 2.28); LODDS2 vs. LODDS0: HR = 3.49, 95% CI (2.88, 4.23)). Meanwhile, LODDS1 and LODDS2 in CRC patients was correlated with poor DFS compared with LODDS0 (LODDS1 vs. LODDS0: HR = 1.82, 95% CI (1.23, 2.68); LODDS2 vs. LODDS0: HR = 3.30, 95% CI (1.74, 6.27)).

Conclusions: The results demonstrated that the LODDS stage was associated with prognosis of CRC patients and could accurately predict the prognosis of patients with CRC.

Keywords: The log odds of positive lymph nodes, Colorectal cancer, Prognosis

Introduction
Colorectal cancer (CRC) is one of the most common malignant tumors in the world, with high morbidity and mortality. It is estimated that there were over 1.8 million new cases in 2018, and at the same time, more than 881,000 deaths were estimated to have occurred [1]. Lymph node (LN) metastasis in patients with CRC is considered a reliable predictor of prognosis and a
The LODDS classification was an excellent independent prognostic factor for patients with CRC, particularly those who had <12 harvested or no lymph node metastasis [23–25]. However, some studies reported that LODDS were not related to the survival of CRC patients [26]. Considering the current controversies regarding the significance of LODDS in the prognosis of CRC patients, we systematically analyzed data obtained in published literature and summed the prognostic significance of LODDS in CRC patients.

Materials and methods

Study selection

We systematically searched PubMed, Medline, Embase, Web of Science and the Cochrane Library for relevant studies from inception to December 3, 2021. The following keywords were used: “log odds of positive lymph nodes”, “Colonic Neoplasms” [Mesh], and “Rectal Neoplasms” [Mesh], “Colorectal Neoplasms” [Mesh]. We used the following strategy: (log odds of positive lymph nodes) OR (LODDS)) AND ((((((“Colonic Neoplasms”[Mesh]) OR (“Rectal Neoplasms”[Mesh])) OR (“Colorectal Neoplasms”[Mesh])) OR (Rectal Neoplasms)) OR (Rectal Cancer)) OR (Rectal Tumor)) OR (Colonic Neoplasms) OR (Colon Cancer)) OR (Colon Tumor)) OR (Colorectal Neoplasms) OR (Colorectal Cancer)) OR (Colorectal Tumor)). For the meta-analysis, we followed PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guidelines [27].

Inclusion and exclusion criteria

Studies fulfilling the following criteria were included: (i) the article reported at least one of the outcomes of interest or the outcome could be calculated according to data extracted from the published data; (ii) only articles published in English, focused on human, and reporting at least one outcome of interest were evaluated, or the outcome could be calculated according to data extracted from the published data; (iii) all CRC patients were diagnosed with the gold standard test; (iv) we included the studies which classified LODDS into three hierarchical levels because currently classification of LODDS has no uniform standard and we found that most of the studies classified LODDS into three categories during the study selection process.

Articles were excluded based on the following criteria: (i) missed crucial information needed for detailed stratification; (ii) number of participants less than 20; (iii) the article was a review, case report, comment, letter, or meeting record; (iv) the article shared a study population with another article.

Data extraction and definitions

Two reviewers independently used a standardized form to extract the data from the included articles: reference, published year, country, type of cancer, number of patients (male/female), age, gender, treatment and prognostic indicators (overall survival (OS) and disease-free survival (DFS)). Any disputes or differences were settled by a third independent investigator. For articles with multiple arms, each arm was considered an independent data set.
Outcomes and quality assessment
Prognostic values (OS and DFS) were used to compare the different LODDS groups.
Two investigators independently assessed the quality of the included articles according to the Newcastle-Ottawa scale (NOS) [28], on the basis of three categories: (i) study group selection; (ii) comparability of groups; and (iii) outcome of interest. The full score was 9, and 1–4 points indicated low-quality, while 5–9 points were considered high-quality.

Data analysis and statistical methods
We used Stata statistical software Version 16.0 (Stata Corporation, College Station, TX) to analyze the data in our meta-analysis. To statistically assess the prognostic effects of LODDS, we extracted the hazard ratio (HR) and 95% confidence interval (CI) of OS and DFS from the included studies. If HRs, 95% CIs, or P values were not directly provided in the original literature, the estimated HR was used to assess prognostic effects based on the method described by Tierney et al. [29], and HR > 1 indicated more disease progression or deaths in the patients. Data were pooled using a random-effects model (REM). All statistical values were combined with 95% CIs and two-sided P values, the threshold of which was set to 0.05. Heterogeneity between articles was calculated using the Q test and I² statistic [30]. For the I² statistic, heterogeneity was defined as low (25–50%), moderate (50–75%) or high (>75%) [31]. For the Q statistic, P ≤ 0.1 was considered to indicate significant heterogeneity. In addition, based on the differences in the data retrieved, subgroup analyses were performed. Then, we also conducted a sensitivity analysis in which each study was removed in turn to evaluate the undue influence of the study on the overall summary estimates including Duval and Tweedie’s trim-and-fill method [32], and Galbraith plots [33]. Publication bias was investigated with qualitative and quantitative methods, including funnel plots and Egger’s test [34]. P values for pooled results were two-sided, and the inspection level was 0.05.

Results
Study characteristics
The original search yielded 204 records in PubMed, Web of Science, Medline, the Cochrane Library and Embase. Of these, 128 duplicate articles were excluded. We excluded 46 records after reading the titles and abstracts. After reviewing the full texts, 10 articles [10–12, 14, 23, 24, 35–38] were finally included in this study. The flowchart of the search and selection process is demonstrated as a PRISMA flowchart in Fig. 1. All articles were published between 2012 and 2021. Overall, the 10 articles included 3523 patients, ranging from 117 to 856 patients. Among these articles, the NOS quality scores ranged from 6 to 7. The characteristics of the selected articles are detailed in Table 1.

Study analysis
We analyzed OS and DFS in different LODDS categories according to the data from the included articles [10–12, 14, 23, 24, 35–38]. The results of the pooled analysis are summarized in Table 2.

OS based on LODDS comparing LODDS0 versus LODDS1 and LODDS2 group
Compared with LODDS0 CRC patients, LODDS1 CRC patients had a worse OS (HR = 1.77, 95% CI (1.38, 2.88)) where the heterogeneity was insignificant (I² statistic = 18.3%, P heterogeneity = 0.280). The pooled results indicated that LODDS2 CRC patients had a worse OS (HR = 3.49, 95% CI (2.88, 4.23)) than LODDS0 CRC patients. Regarding the heterogeneity, there was no statistical significance (I² statistic = 0.0%, P heterogeneity = 0.600), as shown in Fig. 2.

DFS based on LODDS comparing LODDS0 versus LODDS1 and LODDS2 group
Compared with LODDS0 CRC patients, LODDS1 CRC patients had a worse DFS (HR = 1.82, 95% CI (1.23, 2.68)). The heterogeneity was moderate insignificant (I² statistic = 35.0%, P heterogeneity = 0.203). The result of pooled analysis using the random-effects model showed that LODDS2 CRC patients was also associated with poor DFS (HR = 3.30, 95% CI (1.74, 6.27)) than LODDS0 CRC patients, and between-study heterogeneity was obvious (I² statistic = 74.4%, P heterogeneity = 0.002), as shown in Fig. 3.

The source of heterogeneity
To explore the potential sources of heterogeneity, we used Galbraith plot and Duval and Tweedie’s trim-and-fill method to further explore the source of heterogeneity in DFS, and the result showed that the training set of the study by Ogawa T et al. [38] might have mainly contributed substantial heterogeneity to DFS (Fig. 4A). After omitting this study, the pooled HR was not affected obviously (HR = 4.53, 95% CI (3.14, 6.55); Fig. 4B), but the heterogeneity for DFS dropped to an insignificant level (from I² statistic = 74.4%, P heterogeneity = 0.002 to I² statistic = 0.0%, P heterogeneity = 0.948; Fig. 4C).

Subgroup analysis and publication bias
We performed subgroup analysis according to differences in the variables, including the publication year, country, and type of cancer. Consistent with above results,
LODDS1 and LODDS2 CRC patients had a worse OS and DFS compared with LODDS0 CRC patients in most subsets. Although it is found that OS and DFS of non-Asian CRC patients were better than patients from Asian, high LODDS is a marker for poor prognosis both in non-Asian and Asian CRC patients. Meanwhile, although OS and DFS of rectal cancer patients were better than colon cancer patients, high LODDS is a marker for poor prognosis both in colon and rectal cancer patients, as shown in Table 3.

Publication bias was assessed by funnel plots and Egger's test, as shown in Fig. S1. Formal evaluation using Egger's test also failed to identify significant publication bias in the analysis of LODDS1 versus LODDS0 ($p = 0.729$), LODDS2 versus LODDS0 ($p = 0.265$) in OS. Similarly, there was no evidence for significant publication bias in LODDS1 versus LODDS0 ($p = 0.860$), LODDS2 versus LODDS0 ($p = 0.949$) in DFS. The results with heterogeneity adjusted are listed in Table 2. In addition, we used funnel plots to detect publication bias, as shown in Fig. 5. All of the funnel plots of the included articles showed a symmetrical distribution. Thus, no significant publication bias was found in the meta-analyses of OS or DFS.

**Discussion**

To our knowledge, this is the first meta-analysis that focused on the significance of LODDS in the prognosis of CRC patients. Arslan NC [23] suggested that the LODDS classification was an excellent independent prognostic factor for patients with CRC, particularly those who had <12 harvested or no lymph node metastasis. However, Jung W [26] indicated that LODDS were not related to the survival of CRC patients. Our meta-analysis of 10 articles including 3523 patients with CRC indicating that LODDS1 and LODDS2 patients had a worse OS and DFS compared with LODDS0 patients, which showed that LODDS is associated with the prognosis of CRC patients and accurately predicts survival of CRC patients. Compared with LODDS0 CRC patients, LODDS1...
| Reference | Year | Single-center/multicenter | Clinical study design | Country | Patient | Patient number | Age (years) | Population | Follow-up (month) | Follow-up Cutoff | Groups in the study | NOS score |
|-----------|------|----------------------------|-----------------------|---------|---------|----------------|-------------|------------|-------------------|-----------------|-------------------|-----------|
| Arslan NC [23] | 2014 | Single-center prospective | Turkey | 2005-2011 | 440 | 253/167 | Median 66 (18–96) | Underwent curative resection of the colon for primary colon carcinoma | Median 30.6 (0–88) | OS | LODDS0: ≤ −1.36, LODDS1: −1.36 to −0.53, LODDS2: > −0.53 | 182 | 146 | 99 | 8 |
| Baqar AR [35] | 2020 | Single-center retrospective | Australia | 2011-2016 | 856 | 402/454 | Median 73 (22–100) | Consecutive patients treated for colon adenocarcinoma | Median 27.1 (0.1–71) | OS | LODDS0: ≤ −1.36, LODDS1: −1.36 to −0.53, LODDS2: > −0.53 | 569 | 217 | 75 | 8 |
| Fang HY [36] | 2017 | Single-center retrospective | China | 2007-2010 | 192 | 113/79 | Median 59 (23–90) | CRC patients who underwent curative (R0) resection | Median 65 (4–106) | OS | LODDS0: ≤ −0.82, LODDS1: −0.82 to −0.57, LODDS2: > −0.57 | 120 | 17 | 55 | 8 |
| Fortea-Sanchis C [11] | 2018 | Multicenter retrospective | Spain | 2004-2007 | 548 | 296/252 | Median 72 (63–80) | Diagnosed with colon cancer, undergoing surgery with curative intent, and had a complete anatomopathological report | Median 51 (30–64) | OS, DFS | LODDS0: ≤ −2, LODDS1: −2 to 1, LODDS2: > 1 | 349 | 187 | 12 | 8 |
| Lee CW [37] | 2016 | Single-center Retrospective | American | 1995-2013 | 164 | 97/67 | Median 55 (25–95) | Stage III rectal cancer patients who underwent curative resection | NR | OS | LODDS0: ≤ −1.2788, LODDS1: −1.2788 to −0.7105, LODDS2: > −0.7105 | 73 | 43 | 48 | 8 |
| Reference       | Year                  | Study Design | Country | Patient Year | Patient Number | Age (years) | Population | Follow-up (month) | Cutoff | Groups in the Study | NOS Score |
|-----------------|-----------------------|--------------|---------|--------------|----------------|-------------|------------|-------------------|--------|---------------------|-----------|
| Persiani R [24] | 2012                  | Retrospective | Italy   | 2004-2008    | 236            | 98/138      | NC colon cancer patients who had undergone surgical resection | median 26 (2–76) | OS LODDS0: ≤ −1.36 LODDS1: −1.36 to −0.33 LODDS2: > −0.33 | 93 79 42 6 |
| Occhionorelli S [10] | 2018                | Retrospective | Italy   | 2003-2013    | 202            | 98/104      | median 76 underwent urgent colonic resection for complicated colon cancer | mean 64 (1–154) | OS, DFS LODDS0: ≤ −1.36 LODDS1: −1.36 to −0.53 LODDS2: > −0.53 | 89 80 33 8 |
| Ogawa T [38]    | 2015                  | Retrospective | Japan   | 1998-2011    | 117            | 54/63       | Mean ± SD 61 ± 11 Stage IV CRC patients who underwent curative resection | median 51 (4–185) | OS, DFS LODDS0: ≤ −1.133 LODDS1: −1.133 to −0.649 LODDS2: > −0.649 | 39 39 39 8 |
| Scarinci A [14] | 2018                  | Retrospective | Italy   | 2010-2015    | 323            | 172/151     | Mean ± SD 72 ± 11.2 patients with primary colon or rectal adenocarcinoma that underwent curative resection | median 38 (6–67) | OS LODDS0: ≤ −1.36 LODDS1: −1.36 to −0.53 LODDS2: > −0.53 | 165 85 73 8 |
### Table 1 (continued)

| Reference | Year   | Single-center/multicenter | Clinical study design | Country | Patient year | Patient number | Age (years) | Population | Follow-up (mouth) | Follow-up Cutoff | Groups in the study | NOS score |
|-----------|--------|---------------------------|-----------------------|---------|--------------|----------------|-------------|------------|-------------------|-----------------|--------------------|-----------|
| Xu T [References] | 2021   | Single-center             | Retrospective         | China   | 2004-2015    | 445            | Median 55/151 | 23–81     | Patients with locally advanced rectal cancer who received Neoadjuvant chemoradiotherapy and underwent radical surgery | Median 46.7 (12.2–148.7) | DFS LODDS0: ≤ −1.1 LODDS1: −1.1 to −0.6 LODDS2: > −0.6 | 291       |

Abbreviations: CRC Colorectal cancer, HR Hazard ratio, OS Overall survival, DFS Disease-free survival, LODDS Log odds of positive lymph nodes
HR = 1.77, 95% CI (1.38, 2.28)) and LODDS2 (HR = 3.49, 95% CI (2.88, 4.23)) CRC patients had a worse OS with insignificant heterogeneity. Additionally, the pooled results demonstrated that LODDS1 CRC patients had a worse DFS (HR = 1.82, 95% CI (1.23, 2.68)) than LODDS0 CRC patients where the heterogeneity was insignificant. Our pooled analysis also showed that LODDS2 CRC patients was also associated with poor DFS (HR = 4.53, 95% CI (3.14, 6.55)), and between-study heterogeneity was obvious ($I^2$ statistic = 74.4%, P heterogeneity = 0.002). To explore the potential sources of heterogeneity, we used Galbraith plot and Duval and Tweedie's trim-and-fill method to further explore the source of heterogeneity in DFS, and the result showed that the training set of the study by Ogawa T et al. [38] might have mainly contributed substantial heterogeneity to DFS. After omitting this study,
the heterogeneity for DFS dropped to an insignificant level (from $I^2$ statistic = 74.4%, $P_{\text{heterogeneity}} = 0.002$ to $I^2$ statistic = 0.0%, $P_{\text{heterogeneity}} = 0.948$; Fig. 4C), and the pooled HR was not affected obviously (HR = 4.53, 95% CI (3.14, 6.55); Fig. 4B). Most results of the subgroup analysis in our study were in agreement with the survival results described above.

Despite recent advances in novel antitumor therapeutics, the overall survival is far from satisfactory, especially in patients with advanced CRC. To improve the quality of life of oncological patients, it is necessary to accurately estimate prognosis and adopt personalized therapeutics. Although the number-based UICC/AJCC pN classification in patients with radically resected CRC is currently considered as the most reliable predictor of poor prognosis [2, 3], the primary flaw of the pN classification is that the accuracy of the predicting prognosis was significantly influenced by the total number of nodes retrieved [5–7]. Neither the LNR nor pN classification system provided additional prognostic information for patients with N0 status or harvested total lymph nodes (TLNs) < 12. Recently, an increasing number of studies have confirmed the crucial roles of LODDS in the management of several types of cancer, including CRC [39–44]. LODDS, first proposed in breast cancer in which it performed equally well as a prognostic indicator in node-positive and node-negative patients [16], was later generalized to several cancers, including CRC [17–22]. The LODDS classification was a novel prognostic LN-related index that considers the effects of both the numbers of positive LNs and negative LNs.
and gives a new chance to improve the accuracy of pN classification for prognostic assessment, particularly in patients with N0 status or harvested <12 TLNs [45]. By searching the most recent articles considering the prognostic value of LODDS, we found that LODDS is superior to other lymph node–based staging algorithms in predicting prognosis in several cancers. For instance, LODDS demonstrated the highest discriminative capacity and prognostic accuracy for esophageal squamous cell carcinoma (ESCC) patients [46]. Another recent study showed that LODDS was also an independent and superior predictor for OS in head and neck cancer (HNC) in a population-based setting with representative real-life data [47]. However, some studies reported that LODDS were not related to the survival of CRC patients [26]. However, several reasons may be partly explained the inconsistent conclusions of different studies, such as methodological reasons and confounder variables. In view of this, synthesizing all related findings to draw more reliable conclusions would be of interest. To our knowledge, no meta-analysis has examined the significance of LODDS in the prognosis of CRC patients. Therefore, our meta-analysis was the first and most full-scale systematic review and meta-analysis to evaluate the prognostic value of the LODDS in patients with CRC.

However, several limitations of the current meta-analysis should be emphasized. First, because several studies did not report HRs that were estimated based
Second, the optimal cutoff point of LODDS need to be confirmed in a large-scale, international, multicenter prospective study before its promotion for clinical practice. Third, there were an insufficient number of studies to assess the 5-year survival rates of patients with different pN and ratio-based lymph node system (rN) classifications stratified by LODDS. That is, we were not able to access differences in survival among patients in different LODDS classification for patients in each of the pN or rN classifications. Despite these limitations, this is the first meta-analysis of focusing on the crucial roles of LODDS in predicting prognosis of patients with CRC. It is clear that LODDS accurately predicts survival of CRC patients. Moreover, it may be novel prognostic predictor, as a more accurate and sensitive stratification tool for use in clinical studies and in evaluating the appropriateness of chemotherapy treatment in homogenous patient groups.

**Conclusions**

In conclusion, our systematic review demonstrated that LODDS is associated with the prognosis of CRC patients and accurately predicts survival of CRC patients. Our meta-analysis indicated that LODDS1 and LODDS2...
LODDS2 patients have a poorer OS and DFS compared with LODDS0 patients. Moreover, the results of summary analysis demonstrated the significance of LODDS as a remarkable prognostic indicator of OS and DFS in most subgroups. Further high-quality, large-scale, international, well-designed multicenter prospective studies are required to obtain the optimal cutoff point of LODDS until the utilization of LODSS in the clinical practice.

**Abbreviations**
CRC: Colorectal cancer; LODDS: Log odds of positive lymph nodes; CI: Confidence interval; OS: Overall survival; DFS: Disease-free survival; UICC: Union for International Cancer Control; AJCC: American Joint Committee on Cancer; LN: Lymph node; LNR: Lymph node ratio; NOS: Newcastle-Ottawa scale; REM: Random-effects model; HR: Hazard ratio; ESCC: Esophageal squamous cell carcinoma; HNC: Head and neck cancer; GC: Gastric cancer; pN: Pathological N; rN: Ratio-based lymph node.

**Supplementary Information**
The online version contains supplementary material available at https://doi.org/10.1186/s12885-022-09390-x.

**Additional information**
Fig. 5 Assessment of publication bias using Funnel plot analysis. a-b Funnel plot analysis of studies on OS (a) LODDS1 vs. LODDS0, b LODDS2 vs. LODDS0. c-d Funnel plot analysis of studies on DFS (c) LODDS1 vs. LODDS0, d LODDS2 vs. LODDS0. Publication bias was not found in the meta-analyses of OS and DFS. All of the funnel plots of the included articles showed a symmetrical distribution. Thus, no significant publication bias was found in the meta-analyses of OS or DFS. HR, hazard ratio; OS, overall survival; DFS, disease-free survival; LODDS, log odds of positive lymph nodes.

**Acknowledgments**
Not applicable.

**Authors’ contributions**
LYD and WGL: conceived and designed the study, wrote the paper. ZYJ and HB: extracted data. YWL, WXQ, and DLL: searched literatures. DLL and NLR: selected studies. CJF, LJQ, and ZW: performed outcome analysis. LYD, WGL, HL, and FDM: reviewed and edited the manuscript. All authors read and approved the manuscript.
Funding
This project was supported by Project supported by the National Natural Science Foundation of China (No. 82073210), The grant of Shaanxi Province (No. 20192DSF01-02-01) and Xijing Chuzhi Project. The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Availability of data and materials
All data generated or analyzed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
1State key Laboratory of Cancer Biology and National Clinical Research Center for Digestive Diseases, Xijing Hospital of Digestive Diseases, Fourth Military Medical University, 127 Changle West Road, Xi’an, Shaanxi Province 710032, P.R. China. 2School of Aerospace Medicine, Fourth Military Medical University, Xi’an 710032, China. 3Department of Histology and Embryology, School of Basic Medicine, Xi’an Medical University, Xi’an 710021, China. 4Department of Nutrition, Xinqiao Hospital, Army Military Medical University, Chongqing 40038, China.

Received: 10 January 2022   Accepted: 8 March 2022
Published online: 18 March 2022

References
1. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
2. Ovrebo K, Rokke O. Extended lymph node dissection in colorectal cancer surgery. Reliability and reproducibility in assessments of operative reports. Int J Color Dis. 2010;25(2):213–22.
3. Chang GJ, Rodriguez-Bigas MA, Skibber JM, Moyer VA. Lymph node evaluation and survival after curative resection of colon cancer: systematic review. J Natl Cancer Inst. 2007;99(6):433–41.
4. Greene FL. Current TNM staging of colorectal cancer. Lancet Oncol. 2007;8(7):572–3.
5. Nam M, Roy-Chowdhury S, Morgan JW, Lum SS, Wong JH. Quantitating the impact of stage migration on staging accuracy in colorectal cancer. J Am Coll Surg. 2006;203(6):882–7.
6. Desch CE, McNiff KK, Schneider EC, Schrag D, McClure J, Lepisto E, et al. American Society of Clinical Oncology/national comprehensive Cancer network quality measures. J Clin Oncol. 2008;26(21):3631–7.
7. Bilmoria K, Bentrem D, Stewart A, Talamonti M, Winchester D, Kulik K, et al. Lymph node evaluation as a colon cancer quality measure: a national hospital report card. J Natl Cancer Inst. 2008;100(18):1310–7.
8. Vather R, Sammour T, Kahokehr A, Connolly A, Hill A. Lymph node evaluation and long-term survival in Stage II and Stage III colon cancer: a national study. Ann Surg Oncol. 2009;16(3):385–93.
9. Johnson P, Porter G, Ricciardi R, Baxter N. Increasing negative lymph node count is independently associated with improved long-term survival in stage IIIB and IIC colon cancer. J Clin Oncol. 2006;24(22):3570–5.
10. Occhionorelli S, Andreotti D, Vallespi P, Morganti L, Lacavalla D, Forini E, et al. Evaluation on prognostic efficacy of lymph nodes ratio (LNR) and log odds of positive lymph nodes (LODDS) in complicated colon cancer: the first study in emergency surgery. World J Surg Oncol. 2018;16(1):186.
11. Fortea-Sanchis C, Martinez-Ramos D, Escrig-Sos J. The lymph node status as a prognostic factor in colon cancer: comparative population study of classifications using the logarithm of the ratio between metastatic and nonmetastatic nodes (LODDS) versus the pN-TNM classification and ganglion ratio systems. BMC Cancer. 2018;18(1):1208.
12. Xu T, Zhang L, Yu L, Zhu Y, Fang H, Chen B, et al. Log odds of positive lymph nodes is an excellent prognostic factor for patients with rectal cancer after neoadjuvant chemoradiotherapy. Ann Transl Med. 2021;9(8):637.
13. Shen F, Cui JH, Cai K, Pan HQ, Bu HQ, Yu F. Prognostic accuracy of different lymph node staging systems in rectal adenocarcinoma with or without preoperative radiation therapy. Jpn J Clin Oncol. 2018;48(7):625–32.
14. Scarinci A, Di Cesare T, Cavagniglia D, Neri T, Colletti M, Cosenza G, et al. The impact of log odds of positive lymph nodes (LODDS) in colon and rectal cancer patient stratification: a single-center analysis of 325 patients. Updat Surg. 2018;70(1):23–31.
15. Soran A, Ozmen T, Salamat A, Soyibir G, Johnson R. Lymph node ratio (LNR): predicting prognosis after Neoadjuvant chemotheraphy (NAC) in breast Cancer patients. Eur J Breast Health. 2019;15(4):249–55.
16. Vinh-Hung V, Verschraegen C, Promish D, Cserni G, Van de Steene J, Tai P, et al. Ratios of involved nodes in early breast cancer. Breast Cancer Res. 2004;6(6):R680–8.
17. Shi Z, Xiao QZ, Li L, Hu L, Gao YL, Zhao JJ, et al. Application of nomogram containing log odds of metastatic lymph node in gallbladder cancer patients. Ann Transl Med. 2020;8(10):655.
18. Modi KB, Seshan V, Paladini D, Mitra S. Analysis of role of lymph node density, negative lymph node and lodds on survival in cervical cancer. Int J Gynecol Obstet. 2018;143:426–7.
19. Dzedzic D, Rudzinski P, Orłowski T, Surgery T. Log odds as a novel prognostic indicator superior to the number-based and ratio-based category for non-small cell lung cancer. J Thorac Oncol. 2017;12(11):S731.
20. Lin P. Prognostic performance of different lymph node staging systems for esophageal squamous cell carcinoma. Dis Esophagus. 2016;29:157A.
21. Smith DD, Nelson RA, Schwarz RE. A comparison of competing lymph node staging schemes in resectable gastric cancer. Ann Surg Oncol. 2010;17:564.
22. Zhang QW, Zhang CH, Li XB, Ge ZZ. Comparison of three lymph node staging schemes for predicting survival in patients with colorectal cancer: a large population database and Chinese multicenter validation. United European Gastroenterol J. 2018;6(8):A277.
23. Arslan NC, Sokmen S, Canda AE, Terzi C, Sarioglu S. The prognostic impact of the log odds of positive lymph nodes in colon cancer. Color Dis. 2021;23(1):10336–92.
24. Pennisi R, Cananz F, Biondi A, Palani G, Tufo A, Ferrara F, et al. Log odds of positive lymph nodes in colon cancer: a meaningful ratio-based lymph node classification system. World J Surg. 2012;36(3):667–74.
25. Wang J, Hassett J, Dayton M, Kulaylat M. The prognostic superiority of log odds of positive lymph nodes in stage III colon cancer. J Gastrointest Surg. 2008;12(10):1790–6.
26. Jung W, Kim K, Kim J, Shim SJ. Prognostic impact of lymph node ratio in patients undergoing preoperative Chemoradiation therapy followed by curative resection for locally advanced rectal cancer. In vivo. 2020;34(3):1247–53.
27. Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, et al. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P). 2015 statement. Syst Rev. 2015;4:1.
28. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol. 2010;25(9):603–5.
29. Tierney J, Stewar T, Lhersi D, Burdett S, Sydes M. Practical methods for incorporating summary time-to-event data into meta-analysis. Trials. 2007;8:16.
30. Higgins J, Thomas S, Deeks J, Altman D. Measuring inconsistency in meta-analyses. BMJ. 2003;327(7414):557–60.
31. Guyatt G, Oxman A, Kunz R, Woodcock J, Brozek J, Helfand M, et al. GRADE guidelines: 7. Rating the quality of evidence— incorporating probability. J Clin Epidemiol. 2011;64(12):1294–302.
32. Duval S, Tweedie R. Trim and fill: a simple funnel-plot-based method of testing and adjusting for publication bias in meta-analysis. Biometrics. 2000;56(2):455–63.
33. Galbraith R. A note on graphical presentation of estimated odds ratios from several clinical trials. Stat Med. 1988;7(8):889–94.

34. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. BMJ. 1997;315(7109):629–34.

35. Baqar AR, Wilkins S, Wang W, Oliva K, McMurrick P. Log odds of positive lymph nodes is prognostically equivalent to lymph node ratio in non-metastatic colon cancer. BMC Cancer. 2020;20(1):762.

36. Fang HY, Yang H, He ZS, Zhao H, Fu ZM, Zhou FX, et al. Log odds of positive lymph nodes is superior to the number- and ratio-based lymph node classification systems for colorectal cancer patients undergoing curative (R0) resection. Mol Clin Oncol. 2017;6(5):782–8.

37. Lee CW, Wilkinson KH, Sheka AC, Leverson GE, Kennedy GD. The log odds of positive lymph nodes stratifies and predicts survival of high-risk individuals among stage III rectal Cancer patients. Oncologist. 2016;21(4):425–32.

38. Ozawa T, Ishihara S, Sunami E, Kitayama J, Watanabe T. Log odds of positive lymph nodes as a prognostic indicator in stage IV colorectal Cancer patients undergoing curative resection. J Surg Oncol. 2015;111(4):465–71.

39. Zhu J, Hao J, Ma Q, Shi T, Wang S, Yan J, et al. A Novel Prognostic Model and Practical Nomogram for Predicting the Outcomes of Colorectal Cancer: Based on Tumor Biomarkers and Log Odds of Positive Lymph Node Scheme. Front Oncol. 2021;11:661040.

40. Xu Z, Jing J, Ma G. Development and validation of prognostic nomogram based on log odds of positive lymph nodes for patients with gastric signet ring cell carcinoma. Chin J Cancer Res. 2020;32(6):778–93.

41. Che K, Wang Y, Wu N, Liu Q, Yang J, Liu B, et al. Prognostic Nomograms based on three lymph node classification Systems for Resected Gastric Adenocarcinoma: a large population-based cohort study and external validation. Ann Surg Oncol. 2021;28(13):4893–49.

42. Yang X, Huang N, Wang M, Lai H, Wu DJ. Comparison of Different Lymph Node Staging Schemes for Predicting Survival Outcomes in Node-Positive Endometrioid Endometrial Cancer Patients. Front Med (Lausanne). 2021;8:688535.

43. Prassas D, Verde P, Pavljak C, Rehders A, Krieg S, Luedde T, et al. Prognostic Discrimination of Alternative Lymph Node Classification Systems for Patients with Radically Resected Non-Metastatic Colorectal Cancer: A Cohort Study from a Single Tertiary Referral Center. Cancers (Basel). 2021;13(15):3898.

44. Yu Y, Zhang P, Yao R, Wang J, Wang P, Xue X, et al. Prognostic value of log odds of positive lymph nodes in node-positive lung squamous cell carcinoma patients after surgery: a SEER population-based study. Transl Lung Cancer Res. 2020;9(4):1285–301.

45. Tang J, Jiang S, Gao L, Xi X, Zhao R, Lai X, et al. Construction and Validation of a Nomogram Based on the Log Odds of Positive Lymph Nodes to Predict the Prognosis of Medullary Thyroid Carcinoma After Surgery. Ann Surg Oncol. 2021;28(8):4360–70.

46. Wen J, Chen J, Chen D, Jabbour S, Xue T, Guo X, et al. Comprehensive analysis of prognostic value of lymph node classifications in esophageal squamous cell carcinoma: a large real-world multicenter study. Ther Adv Med Oncol. 2021;13:7588359211054895.

47. Wen J, Wei Y, Jabbour S, Xu T, Wang Y, Chen J, Wang J, Hu C, Su F, Fan M, et al. Comprehensive analysis of prognostic value of lymph node staging classifications in patients with head and neck squamous cell carcinoma after cervical lymph node dissection. Eur J Surg Oncol. 2021;47(7):1710–7.

Publisher's Note
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.