INPLASY

Lymph Node Metastasis Risk Factors in T1 Colorectal Cancer After Endoscopic Resection: A Systematic Review and Meta-analysis

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

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 17 June 2026 and was last updated on 17 June 2026.

INTRODUCTION

Review question / Objective Review question

Among patients with pathologically confirmed T1 colorectal cancer who undergo endoscopic resection, which clinicopathological characteristics are associated with lymph node metastasis?

Objective

The objective of this systematic review and meta-analysis is to comprehensively evaluate the associations between major clinicopathological features and lymph node metastasis (LNM) in T1 colorectal cancer after endoscopic resection. Specifically, we aim to quantify the effects of lymphovascular invasion, lymphatic invasion, venous/vascular invasion, tumour budding, histological differentiation, depth of submucosal invasion, and tumour location on the risk of LNM.

In addition, we aim to compare the relative strength of these pathological risk factors and establish a clinically interpretable hierarchy of risk. The findings of this review will provide evidence to support postoperative risk stratification and decision-making regarding additional radical surgery following endoscopic treatment of T1 colorectal cancer.

PICOS framework

Population (P):
Patients with pathologically confirmed T1 colorectal cancer treated with endoscopic resection.

Exposure (I):
Presence of clinicopathological risk factors, including lymphovascular invasion, lymphatic invasion, venous/vascular invasion, tumour budding, poor differentiation/high-grade histology, deep submucosal invasion, and tumour location.

Comparator (C):
Absence of the corresponding clinicopathological risk factor.

Outcome (O):
Histologically confirmed lymph node metastasis.

Study design (S):
Observational studies, including retrospective or prospective cohort studies and case-control studies, reporting associations between clinicopathological characteristics and lymph node metastasis in T1 colorectal cancer.

Rationale T1 colorectal cancer represents an early stage of colorectal cancer in which tumour invasion is limited to the submucosa. Endoscopic resection is increasingly used as a minimally invasive treatment; however, a proportion of patients harbour occult lymph node metastasis and may require additional radical surgery with lymphadenectomy.

Current international guidelines recommend additional surgery when certain pathological high-risk features are present, including lymphovascular invasion, poor differentiation, tumour budding, and deep submucosal invasion. Nevertheless, the relative importance of these risk factors remains uncertain. Existing studies have reported inconsistent results, and the magnitude of risk associated with individual pathological features varies considerably across studies. Furthermore, some risk factors included in current guidelines may not contribute equally to lymph node metastasis risk.

A comprehensive quantitative synthesis of the available evidence is therefore needed. By systematically evaluating the associations between major clinicopathological characteristics and lymph node metastasis, this review aims to provide more robust evidence regarding the strength of individual risk factors. The results may help improve postoperative risk stratification and support more individualized decisions regarding additional surgery after endoscopic resection of T1 colorectal cancer.

Condition being studied T1 colorectal cancer (T1 CRC) and lymph node metastasis.

T1 colorectal cancer is defined as colorectal adenocarcinoma with invasion into the submucosal layer but without extension beyond the muscularis propria. Although endoscopic resection is considered curative for many patients, a subset of cases harbour lymph node metastasis, which remains the most important determinant of the need for additional surgical treatment. This review focuses on clinicopathological factors associated with lymph node metastasis in patients with T1 colorectal cancer.

METHODS

Search strategy A systematic literature search was conducted in PubMed, Web of Science, and Embase from database inception to June 2026.

The PubMed search strategy was as follows:

("Colorectal Neoplasms"[Mesh] OR colorectal cancer[Title/Abstract] OR colorectal carcinoma[Title/Abstract] OR colon cancer[Title/Abstract] OR colon carcinoma[Title/Abstract] OR rectal cancer[Title/Abstract] OR rectal carcinoma[Title/Abstract] OR colorectal neoplasm*[Title/Abstract])
AND
(T1[Title/Abstract] OR pT1[Title/Abstract] OR "T1 colorectal cancer"[Title/Abstract] OR "T1 colorectal carcinoma"[Title/Abstract] OR "pT1 colorectal cancer"[Title/Abstract] OR "pT1 colorectal carcinoma"[Title/Abstract] OR "early colorectal cancer"[Title/Abstract] OR "early-stage colorectal cancer"[Title/Abstract] OR "submucosal invasive colorectal cancer"[Title/Abstract] OR "submucosal invasion"[Title/Abstract])
AND
("Endoscopic Mucosal Resection"[Mesh] OR endoscopic resection[Title/Abstract] OR endoscopic mucosal resection[Title/Abstract] OR EMR[Title/Abstract] OR endoscopic submucosal dissection[Title/Abstract] OR ESD[Title/Abstract] OR local excision[Title/Abstract])
AND
(lymph node metastasis[Title/Abstract] OR lymph node metastases[Title/Abstract] OR nodal metastasis[Title/Abstract] OR nodal metastases[Title/Abstract] OR lymphatic metastasis[Title/Abstract] OR LNM[Title/Abstract])

The Web of Science search strategy was:

TS=(("T1 colorectal cancer" OR "T1 colorectal carcinoma" OR "pT1 colorectal cancer" OR "pT1 colorectal carcinoma" OR "pT1 CRC" OR "T1 colon cancer" OR "T1 rectal cancer" OR "early colorectal cancer" OR "early-stage colorectal cancer" OR "submucosal invasive colorectal cancer" OR "submucosal invasion")
AND
("endoscopic resection" OR "endoscopic mucosal resection" OR EMR OR "endoscopic submucosal dissection" OR ESD OR "local excision")

AND
("lymph node metastasis" OR "lymph node metastases" OR "nodal metastasis" OR "nodal metastases" OR "lymphatic metastasis" OR LNM))

The Embase search strategy was:

('t1 colorectal cancer' OR 't1 colorectal carcinoma' OR 'pt1 colorectal cancer' OR 'pt1 colorectal carcinoma' OR 't1 colon cancer' OR 't1 rectal cancer' OR 'early colorectal cancer' OR 'early-stage colorectal cancer' OR 'submucosal invasive colorectal cancer'/exp OR 'submucosal invasion')
AND
('endoscopic resection'/exp OR 'endoscopic resection' OR 'endoscopic mucosal resection'/exp OR 'endoscopic mucosal resection' OR 'emr' OR 'endoscopic submucosal dissection'/exp OR 'endoscopic submucosal dissection' OR 'esd' OR 'local excision'/exp OR 'local excision')
AND
('lymph node metastasis'/exp OR 'lymph node metastasis' OR 'nodal metastasis'/exp OR 'nodal metastasis' OR 'lymphatic metastasis'/exp OR 'lymphatic metastasis')

Only studies published in English and involving human subjects were considered where applicable. Reference lists of relevant articles were manually screened to identify additional eligible studies.

Participant or population Patients with pathologically confirmed T1 colorectal cancer who underwent endoscopic resection and had pathological evaluation of lymph node status following surgical resection.

Intervention Presence of clinicopathological risk factors, including lymphovascular invasion, lymphatic invasion, venous/vascular invasion, tumour budding, poor differentiation/high-grade histology, deep submucosal invasion, and tumour location.

Comparator Absence of the corresponding clinicopathological risk factor.

Study designs to be included Observational studies, including retrospective cohort studies, prospective cohort studies, and case-control studies reporting associations between clinicopathological factors and lymph node metastasis in T1 colorectal cancer.

Eligibility criteria Inclusion criteria:

1. Studies including patients with pathologically confirmed T1 colorectal cancer.
2. Studies reporting clinicopathological risk factors associated with lymph node metastasis.
3. Studies providing sufficient data to construct 2×2 contingency tables or calculate effect estimates.
4. Full-text articles published in English.

Exclusion criteria:

1. Reviews, editorials, letters, comments, conference abstracts, case reports, and case series with fewer than 10 patients.
2. Studies without extractable data.
3. Duplicate publications or overlapping cohorts.
4. Non-human studies.
5. Articles not published in English.

Information sources Electronic searches will be performed in PubMed and Web of Science. Additional studies will be identified through manual screening of reference lists from eligible articles and relevant review articles.

Main outcome(s) The primary outcome is histologically confirmed lymph node metastasis in patients with T1 colorectal cancer.
Pooled odds ratios (ORs) with 95% confidence intervals (CIs) will be calculated for each clinicopathological risk factor.

Additional outcome(s) Adjusted effect estimates reported in multivariable analyses will be pooled separately when sufficient data are available.
Heterogeneity, publication bias, and robustness of findings will also be evaluated.

Data management Two reviewers will independently screen studies, extract data, and verify eligibility. Extracted information will include study characteristics, patient demographics, tumour characteristics, pathological risk factors, lymph node metastasis outcomes, and effect estimates. Any disagreements will be resolved through discussion or consultation with a third reviewer.

Quality assessment / Risk of bias analysis Methodological quality of included observational studies will be assessed using the Newcastle–Ottawa Scale (NOS). Studies will be evaluated in the domains of selection, comparability, and outcome assessment. Risk of bias assessments will be performed independently by two reviewers.

Strategy of data synthesis Meta-analyses will be conducted using random-effects models. Pooled

odds ratios (ORs) and 95% confidence intervals (CIs) will be calculated for each clinicopathological factor.

Statistical heterogeneity will be assessed using Cochran's Q test and the I^2 statistic. Publication bias will be evaluated using funnel plots and Egger's test when sufficient studies are available. Separate analyses will be performed for lymphovascular invasion, lymphatic invasion, venous/vascular invasion, tumour budding, poor differentiation/high-grade histology, submucosal invasion depth, and tumour location. Adjusted estimates will be synthesized separately when possible.

Subgroup analysis Where sufficient studies are available, subgroup analyses will be conducted according to study region, tumour location (colon versus rectum), and pathological assessment methods.

Sensitivity analysis Sensitivity analyses will be performed using leave-one-out analyses to evaluate the influence of individual studies on pooled estimates. Additional analyses excluding studies at higher risk of bias may be conducted where appropriate.

Language restriction Only studies published in English were included.

Country(ies) involved China.

Other relevant information This review will be conducted and reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Keywords T1 colorectal cancer; lymph node metastasis; endoscopic resection; tumour budding; lymphovascular invasion; meta-analysis.

Dissemination plans T1 colorectal cancer; lymph node metastasis; endoscopic resection; tumour budding; lymphovascular invasion; meta-analysis.

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