INTRODUCTION

Review question / Objective: Early gastric cancer (EGC) refers to mucosal and submucosal involvement, and its 5-year survival rate is greater than 90% regardless of lymph node status (T1Nx). Minimally invasive surgery is becoming more and more popular in the treatment of early gastric cancer. Endoscopic resection (ER) includes endoscopic mucosal resection (endoscopic mucosal resection). EMR and endoscopic submucosal dissection (ESD) are minimally invasive procedures for EGC with low risk lymph node metastasis. It is comparable to surgery in terms of postoperative survival rate and other long-term outcomes, but significantly better than surgery in terms of postoperative hospital stay, cost, quality of life and long-term complications. However, for early gastric cancer with lymph node metastasis, the radical effect cannot be achieved. It is reported that 0.9% of patients with absolute indication of ESD need subsequent gastrectomy, and 19.2% of patients with expanded indication of ESD need subsequent gastrectomy. Residual cancer and lymph node metastases were detected in subsequent gastrectomy specimens in 5.6% to 11.5% and 7.5% to 16.7%, respectively. Therefore, only by accurately predicting lymph node metastases can unnecessary gastrectomy after ESD be avoided. Therefore, our objective is to determine the risk factors for lymph node metastasis in patients with early gastric cancer by systematic review and meta-analysis of related studies, so as to provide a basis for formulating a reasonable treatment plan for patients with early gastric cancer.
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**Condition being studied:** At present, for EGC patients without lymph node metastasis, preserving function or organs to improve postoperative quality of life has become the focus of treatment. The evaluation of the risk of lymph node metastasis is the key to the choice of treatment for early gastric cancer. The accurate assessment of the risk of lymph node metastasis in patients with EGC is not known because the occurrence of lymph node metastasis is relatively rare. In addition, the findings regarding some risk factors for lymph node metastasis have not been consistent in other studies. Therefore, our objective is to determine the risk factors for lymph node metastasis in patients with early gastric cancer by systematic review and meta-analysis of related studies, so as to provide a basis for

**METHODS**

**Search strategy:** 5. Foreign language database: Pubmed: (The remaining 1-4 have no Chinese retrieval strategy and cannot be uploaded due to the word limit)

Type of disease: lymph node metastasis of early gastric cancer

Early gastric cancer subject words:
- Stomach Neoplasms,
- Free word:
  - Neoplasm, Stomach
  - Stomach Neoplasm
  - Neoplasms, Stomach
  - Gastric Neoplasms
  - Gastric Neoplasm
  - Neoplasm, Gastric
  - Neoplasms, Gastric
  - Cancer of Stomach
  - Stomach Cancers
  - Gastric Cancer
  - Cancer, Gastric
  - Cancers, Gastric
  - Gastric Cancers
  - Stomach Cancer
  - Cancer, Stomach
  - Cancers, Stomach
  - Cancer of the Stomach
  - Gastric Cancer, Familial Diffuse

early gastric cancer

EGC

Lymph node subject words: Lymph Nodes
- Free word:
  - Lymph Node
  - Node, Lymph
  - Nodes, Lymph
  - lymph node metastasis

Metastasis subject words: Neoplasm
- Metastasis,
- Free word:
  - Neoplasm Metastases
  - Metastases, Neoplasm
  - Metastasis, Neoplasm
  - Metastase
  - Metastases
  - Metastasis
- Causation:
  - Influencing factors or risk factors or etiology or related factors:
Causation standard retrieval form:
(relative>Title/Abstract) AND risk>Title/Abstract) OR(relative risk>Title/Abstract) OR risks>Title Word) OR cohort studies[MeSH:noexp] OR (cohort>Title/Abstract) AND stud>Title/Abstract)
pubmed:
Search: ((("Stomach Neoplasms"[Mesh]) OR (((((Neoplasm, Stomach) OR (Stomach Neoplasm)) OR (Neoplasms, Stomach)) OR (Gastric Neoplasms)) OR (Gastric Neoplasm)) OR (Neoplasm, Gastric)) OR (Neoplasms, Gastric)) OR (Cancer of Stomach)) OR (Stomach Cancers)) OR (Cancer, Gastric)) OR (Cancers, Gastric)) OR (Cancer of the Stomach)) OR (Gastric Cancer)) OR (Cancer, Gastric) Explode all trees 2911
#2 (Neoplasm, Stomach):ab,ti,kw or (Stomach Neoplasm):ab,ti,kw or (Neoplasms, Stomach):ab,ti,kw or (Gastric Neoplasms):ab,ti,kw or (Gastric Neoplasm):ab,ti,kw or (Neoplasm, Gastric):ab,ti,kw or (Neoplasms, Gastric):ab,ti,kw or (Cancer of Stomach):ab,ti,kw or (Stomach Cancers):ab,ti,kw or (Gastric Cancer):ab,ti,kw or (Cancer, Gastric):ab,ti,kw or (Cancers, Gastric):ab,ti,kw or (Gastric Cancers):ab,ti,kw or (Stomach Cancer):ab,ti,kw or (Cancer of the Stomach):ab,ti,kw or (Gastric Cancer, Familial Diffuse):ab,ti,kw or (early gastric cancer):ab,ti,kw or (EGC):ab,ti,kw
#3 #1 or #2 10739
#4 MeSH descriptor: [Lymph Nodes] explode all trees 907
#5 (Lymph Node):ab,ti,kw or (Node, Lymph):ab,ti,kw or (Nodes, Lymph):ab,ti,kw or (lymph node metastasis):ab,ti,kw
#6 #4 or #5 12970
#8 (Neoplasm Metastases):ab,ti,kw or (Metastases, Neoplasm):ab,ti,kw or (Metastasis, Neoplasm):ab,ti,kw or (Metastases[Title/Abstract])) OR (Metastases[Title/Abstract])) OR (Metastasis[Title/Abstract])) OR (Metastasis[Title/Abstract])) OR (relative>Title/Abstract) AND risk>Title/Abstract) OR (relative risk>Title/Abstract) OR risks>Title Word) OR cohort studies[MeSH:noexp] OR (cohort>Title/Abstract) AND stud>Title/Abstract))
#9 #7 or #8 27860
#10 #6 or #9 35367
#11 (relative risk):ab,ti,kw OR (cohort studies):ab,ti,kw
#12 #3 and #10 and #11 69
8.Web of Science:
https://www.webofscience.com/wos/alldb/summary/95c5dd09-1828-4bb8-bbff-3bc44aa4192-52f2bcef/relevance/1

Participant or population: Lymph node metastasis of early gastric cancer.

Intervention: Risk factors.
Comparator: Patients with early gastric cancer without lymph node metastasis

Study designs to be included: Case-control study or cohort study

Eligibility criteria: Inclusion criteria:(1) Case-control study or cohort study designed as risk factors for lymph node metastasis in early gastric cancer; (2) The original data, OR value, 95%CI OR convertible OR value, 95%CI are provided; (3) Papers published from January 1, 2010 to October 1, 2022 and published in SCI or Chinese core science and technology journals. Exclusion criteria:(1) Review literature, abstract only, no control group, original studies with sample size < 100; (2) only specific types of gastric cancer were studied; (3) The definition of risk factors is not accurate, and the full text of the literature cannot be obtained. (4) The main research objects were people before 2010.

Information sources: Web Of Science database, Pubmed database, Embase database, Cochrane Library, Chinese databases (CNKI, Wanfang, CBM, VIP)

Main outcome(s): Risk factors for lymph node metastasis in early gastric cancer: Lymphatic invasion, vascular invasion, undifferentiated type, Invasion depth of submucosa ≥500 μm, Morphological ulcer, Sex factor, Tumor diameter

Quality assessment / Risk of bias analysis: Our study followed the MOOSE reporting specification. The quality of each study that met the inclusion criteria was assessed using the Newcastle-Ottawa scale (NOS), with scores ranging from 0 to 9, with a total score of ≥6 indicating high quality studies.

Strategy of data synthesis: RevMan 5.3 and Stata14 were used to merge the extracted data. Pooled results were expressed as odds ratios (ORs) and 95% confidence intervals (95%CI). Q test and I2 analysis were used to evaluate the heterogeneity among the included studies [8]. When p > 0.1 and I2 < 50%, it indicated that there was no statistical heterogeneity among the studies, and the data were analyzed using the fixed-effect model. In addition, we used sensitivity analysis to test for heterogeneity and excluded relevant articles contributing to heterogeneity. If heterogeneity could not be excluded, a random effects model was used. A bias test is also required. P < 0.05 was considered statistically significant.

Subgroup analysis: No subgroup findings yet.

Sensitivity analysis: After deleting any one of the papers, the combined results of the remaining papers are not different from those without deletion, which means that sensitivity analysis has been passed.

Country(ies) involved: China.

Keywords: Early gastric cancer; Lymph node metastasis; Risk factor; Meta-analysis.

Contributions of each author: Author 1 - Ailimulatijiang Yilihamu. Author 2 - Ying Bin Cai.