INTRODUCTION

Review question / Objective: Esophageal invasion is a significant predictor for lower mediastinal lymph node (LMLN) metastasis in carcinoma of esophagogastric junction (EGJ). The role between esophageal invasion length (EIL) and LMLN involvement still is a debate in EGJ carcinoma. This systemic review aim to review and summarize the incidence of LMLN metastasis or recurrence base on different EIL in EGJ carcinoma.

Eligibility criteria: Studies were included base on the following criteria: histologically confirmed EGJ carcinoma, underwent LMLN dissection and report the involvement rate of LMLN, report the EIL in centimeters and LMLN involvement rate in different EIL and case numbers in each EIL group. Analysis base on other studies, not English articles, reviews, case reports, data inconsistent, EIL wasn’t subgrouped in centimeters and mediastinal lymph node was’s subgrouped are exclusion criteria.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 May 2022 and was last updated on 26 May 2022 (registration number INPLASY202250147).

CONFLICTS OF INTEREST:
None declared.
review and summarize the incidence of LMLN metastasis or recurrence base on different EIL in EGJ carcinoma.

**Condition being studied:** Many researches had reported that the incidence of adenocarcinoma of esophagogastric junction (AEG) is increasing over the years. Anatomically, AEG crosses the esophagus and proximal stomach, which indicate the lymphatic drainage and treatment of AEG has the characteristic of both stomach and esophageal carcinoma. AEG was classified base on central tumor location for further specified treatment as follows: Type I, tumor center is located between 1 and 5 cm proximal to EGJ; Type II, tumor center is located between 1 cm proximal to and 2 cm distal from the EGJ; and Type III, the tumor center is located between 2 and 5 cm distal from the EGJ with esophageal invasion and it has been widely used worldwide. Radical surgery is still the main treatment for AEG. However, there are still several controversials in the surgical treatment of Siewert type II AEG, such as area of lymph node dissection, reconstruction and surgical approach ect. Esophageal invasion length is significant predictive factor for lymph node metastasis and prognosis. Some researchers reported the mediastinal lymph node metastasis in different EIL these years. Koyonagi et al reported the estimated 5-year overall survival rates for the ≤25 mm EIL group and the >25 mm EIL group were 66.8% and 40.9%, respectively, and the LMLN involvement rate is increasing from 2.7% in 0-9mm EIL group to 39.1% in 30-39mm EIL group. It's important to determine the pattern of EIL and mediastinal lymph node metastasis and whether a LMLN dissection should be made in different esophageal invasion AEG patient. However, no systemic review has been made to summarize how EIL effect on LMLN involvement. Therefore, in order to provide an evidence about incidence of LMLN involvement on different EIL in EGJ carcinoma, a systemic review and meta-analysis of the literature was made, which should be important for guidance for LMLN dissection.

**METHODS**

**Search strategy:** Pubmed: ((Gastroesophageal Junction[MeSH Terms]) OR (Gastroesophageal Junction[All Fields]) OR (esophagogastric junction[All Fields]) OR ("cardia"[All Fields])) AND ((adenocarcinomas[MeSH Terms]) OR (adenocarcinomas[All Fields]) OR ("neoplasms"[All Fields]) OR ("carcinoma"[All Fields])) AND ((Lymph Node Metastasis[MeSH Terms]) OR (Lymph Node Metastasis[All Fields]) OR ("lymph node mapping"[All Fields]))

Embase ('gastroesophageal junction'/exp OR 'cardia'/exp) AND (adenocarcinomas OR 'neoplasm'/exp OR 'carcinoma'/exp) AND ('lymph node metastasis'/exp OR 'lymph node mapping'/exp) And cochrane is searched as well.

**Participant or population:** EGJ carcinoma patients.

**Intervention:** Different esophageal invasion length.

**Comparator:** lower mediastinal lymph node involvement rate.

**Study designs to be included:** There were no restrictions on study design.

**Eligibility criteria:** Studies were included base on the following criteria: histologically confirmed EGJ carcinoma, underwent LMLN dissection and report the involvement rate of LMLN, report the EIL in centimeters and LMLN involvement rate in different EIL and case numbers in each EIL group. Analysis base on other studies, not English articles, reviews, case reports, data inconsistent, EIL wasn't subgrouped in centimeters and mediastinal lymph node was's subgrouped are exclusion criteria.

**Information sources:** Data is searched through electronic databases: 1. pubmed; 2. embase; 3. cochrane. Time span in studies isn't limited.

**Main outcome(s):** Main outcomes: 8 studies with 1237 patients were included. The histological type is adenocarcinoma(AC) in...
1180 cases (95.4%) and squamous cell carcinoma (SCC) in 57 cases (4.6%). The neoadjuvant therapy was given to 199 patients (16.1%). The incidence of LMLN involvement in EIL:0-1cm group is 2% [95% CI, 0%-4%] in 5 studies with 316 patients, 6% [95% CI, 3%-9%] in EIL:1-2cm group in 6 studies with 265 patients, 16% [95% CI, 12%-22%] in EIL:2-3cm group in 8 studies with 217 patients and 27% [95% CI, 22%-33%] in EIL>3cm group in 8 studies with 229 patients.

**Quality assessment / Risk of bias analysis:** The quality of all selected articles was scored according to the Agency for Healthcare Research and Quality (AHRQ).

**Strategy of data synthesis:** Single Proportion of meta-analysis is used.

**Subgroup analysis:** We only described the LMLN involvement rate in different EIL. There will be no subgroup analysis.

**Sensitivity analysis:** None.

**Language:** English.

**Country(ies) involved:** China.

**Keywords:** Esophagogastric Junction; Lower Mediastinal Lymph Node; Meta-analysis.

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