Original Article

Systematic review and meta-analysis of endoscopic ultrasonography in staging diagnosis of esophageal cancer after neoadjuvant radiotherapy and chemotherapy

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Background: Clinically, it is necessary to evaluate the overall situation of the tumor before treatment, understand the disease stage of the patient, and choose the most reasonable treatment plan. Therefore, it is necessary to seek an efficient and accurate staging diagnosis method. Endoscopic ultrasonography (EUS) is widely used in staging esophageal cancer, but its accuracy will be affected by the experience of endoscopic diagnosis physicians.

Methods: Computer retrieval PubMed, MEDLINE, EBSCO, Science Direct, Cochrane Library, China National Knowledge Infrastructure (CNKI). Relevant literatures published from the database establishment to January 2022 were searched using "Endoscopic ultrasound, esophageal cancer, neoadjuvant chemotherapy, diagnosis, tumor node metastasis" as the detection term. Quality assessment of diagnostic accuracy studies (QUADAS) was used to evaluate the quality of the included literatures, Q test and heterogeneity (I2) was adopted to evaluate the heterogeneity among various studies, and the sensitivity and specificity of EUS were calculated and compared in evaluating various stages of esophageal cancer.

Results: A total of 12 articles and 824 patients were included. 12 literatures on EUS in diagnosis of T staging were included for heterogeneity test, the combined sensitivity of T1–T4 stage was 0.16 (95% CI: 0.05–0.39), 0.34 (95% CI: 0.20–0.52), 0.78 (95% CI: 0.63–0.88), 0.16 (95% CI: 0.04–0.50). The combined specificity was 0.99 (95% CI: 0.94–1.00), 0.52 (95% CI: 0.36–0.68), 0.98 (95% CI: 0.95–0.99). According to the heterogeneity test of EUS n staging in 9 literatures, the combined sensitivities of N0-N1 stage was 0.62 (95% CI: 0.53–0.71) and 0.65 (95% CI: 0.58–0.72), combined specificities was 0.65 (95% CI: 0.58–0.71) and 0.63 (95% CI: 0.54–0.72).

Discussion: Based on the results, EUS is not a good diagnostic test for TNM staging.

Keywords: Esophageal cancer; neoadjuvant chemotherapy; endoscopic ultrasound; diagnosis of therapeutic effects; meta-analysis

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Introduction

Esophageal cancer, as a common malignant tumor of digestive tract, has a high morbidity and mortality rate (1,2). Because of its insidious onset and high malignancy, patients are often in the advanced stage at the time of seeing a doctor, and sometimes other parts are found to be invaded during surgery, so radical resection cannot be performed (3-5). Therefore, it is very important to accurately evaluate the preoperative staging of patients. For esophageal cancer patients, accurate preoperative staging is helpful to provide the most appropriate individualized treatment plan for these patients (6-10). For example, some patients with preoperative stage T4 can increase the chance of radical resection through neoadjuvant therapy (11,12). For patients with T1, N0 and M0 stages, especially those with high surgical risk, endoscopic mucosal resection or endoscopic submucosal dissection can avoid the possible complications of surgical treatment and strive for radical treatment with minimal trauma (13-15).

At present, the most commonly used methods for preoperative staging of esophageal cancer mainly include computed tomography (CT), endoscopic ultrasonography (EUS) and positron emission tomography (PET) (16-21). Among them, CT, especially enhanced CT, is the most commonly used examination method to exclude distant metastasis of esophageal cancer patients, which can accurately find the most common liver, brain and lung metastasis (21,22). However, it has a limited role in judging the accurate depth of tumor invasion into esophageal wall, and the accuracy of evaluating T staging is poor (23). PET is more sensitive than CT in the diagnosis of primary tumors, but its limited information on the depth of tumor invasion limits its role in T staging (24,25). EUS is a gastrointestinal tract examination technology that combines an endoscope and ultrasound, and it plays a vital role in the staging of esophageal cancer and determination of the origin and depth of tumors (26,27). In terms of the structure of EUS, a miniature high-frequency ultrasonic probe is installed on the top of the endoscope, and an ultrasonic scan can be performed by the endoscope entering the body to obtain the ultrasonic images of the features of gastrointestinal tissue. The obtained images can be of some help to more intuitive and accurate diagnosis of disease and the implementation of follow-up targeted treatment plans (28,29). EUS can measure the diameter and cross-sectional area of the esophageal wall and the gastric wall by ultrasound. A study (30) indicates that the percentage of the reduction in the maximum cross-sectional area of EUS is closely related to the efficacy of neoadjuvant therapy. If the maximum cross-sectional area of EUS is reduced by over 50%, neoadjuvant chemotherapy is effective for tumors.

This study was innovatively incorporated into the current literature research on EUS in evaluating the staging of esophageal cancer after neoadjuvant chemotherapy at home and abroad, and evaluated the diagnostic ability of EUS in staging of esophageal cancer after neoadjuvant chemotherapy through meta-analysis system, so as to evaluate the reference value of EUS in the analysis and diagnosis of esophageal cancer, and provide theoretical reference for clinical diagnosis of preoperative staging of esophageal cancer. We present the following article in accordance with the PRISMA-DTA reporting checklist (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-437/rc).

Methods

Article retrieval

PubMed, this paper uses computer to search PubMed, MEDLINE, EBSCO, Science Direct, Cochrane Library and CNKI. With "ethical ultrasound, esophageal cancer, neo adjuvant chemotherapy, diagnosis, tumor node metastasis" as the detection words, the relevant literatures published from the database establishment to January 2022 were searched manually, and professional journals were searched to avoid omissions. In addition, the research object of the literature search was human beings.

In the retrieval process, subject words and free words were combined to carry out multiple retrievals to obtain the references that could be included. After that, a search engine was used to trace each article. Rev Man 5.3 software provided by Cochrane collaboration network was used to evaluate the risk of inclusion in the literature.

Article inclusion and exclusion criteria

The articles were included based on the following criteria:

(I) Patients were engaged in the study on neoadjuvant chemotherapy before surgery;
(II) Histopathological diagnostic result was the gold standard;
(III) Patients were adults over 18 years old;
(IV) True positive, false positive, false negative, and true negative values of staging diagnosis could be

obtained directly or indirectly;

(V) Articles were published in English language.

The articles were excluded based on the following criteria:

(I) Articles were case reports, overviews, conferences, letters, and reviews;

(II) Histopathological features were not the gold standard;

(III) The research objects were animals or *in vitro* study was involved;

(IV) There was no sufficient data determining diagnostic indexes in articles;

(V) TNM classification system was not used to conduct the study on esophageal cancer staging.

Data extraction

Two professionals used uniform Microsoft Excel (Microsoft, the United States) to screen articles and extract data independently. The main data extracted include the final results. If there was a disagreement, they resolved it by discussion. The main extracted data were as follows:

(I) General data included in articles, such as title, first author, and publication year;

(II) The basic features of research objects, including sample size and detection methods;

(III) Diagnostic index test results;

(IV) The detection rate of esophageal cancer patients at each stage after neoadjuvant chemotherapy in each article and the data that determined the accuracy of tests (sensitivity and specificity).

Evaluation criteria of articles

Quality assessment of diagnostic accuracy studies (QUADAS) recommended by Cochrane (the United States) criteria was adopted to evaluate the quality of the included articles. According to each evaluation index, the quality of the original included articles was evaluated. Each article was evaluated as "yes", "no", or "uncertain".

Statistical methods

Rev Man 5.3 software (Cochrane, the United States) and Stata software (Stata Corp, the United States) were used to draw the bias risk assessment map. Furthermore, Q-test and heterogeneity (I^2) were used to evaluate the heterogeneity among each article. The sensitivity and specificity of the assessment of each esophageal cancer stage using EUS were calculated, compared, and expressed by 95% confidence interval (CI). In addition, forest plots and summary receiver operating characteristic (SROC) curves were drawn. Funnel plots of different diagnostic indexes were adopted to test potential publication bias and carry out sensitivity analysis.

Results

Retrieval results and basic information about articles

A total of 211 articles were obtained by database retrieval [173] and manual journal retrieval [38]. In 173 articles, 4 articles were duplicates and 68 disqualified articles were excluded. Furthermore, 11 articles were also excluded for other reasons (There is a problem with the statistical method, the sample size is too small). The remaining 90 articles were initially selected. After that, 32 articles (there is content in the abstract and title that is not relevant to this article) were excluded by reading abstracts and titles, and there were 58 remaining articles. In addition, 29 research reports and review articles were excluded, and there were 29 remaining articles. By reading the full-text of all remaining articles, 12 articles with incorrect research types were excluded, and 4 articles were also excluded because the required diagnostic results were incomplete or unavailable. TNM staging criteria were not used in 1 article, so this article was excluded Finally, a total of 12 articles were included in meta-analysis. In 38 articles, 25 research reports and review articles were excluded, and there were 13 remaining articles. By reading the full-text of all remaining articles, 4 articles with incorrect research types were excluded, 7 articles with incorrect research types were excluded, and 2 articles were also excluded because the required diagnostic results were incomplete or unavailable. *Figure 1* shows the process of article retrieval.

By reading the content of the included articles, the basic information about the articles was extracted. Among the 12 included articles, there were 824 patients receiving esophageal cancer neoadjuvant chemotherapy, and the sample size ranged from 17 to 143. In the 12 included articles, each index of the preoperative diagnostic staging for esophageal cancer patients using EUS after neoadjuvant chemotherapy was described in detail. Furthermore, vital histopathological staging diagnostic results were the gold standard in all 12 articles. In 11 articles, T1, T2, and T3 patients were involved, T4 esophageal cancer patients were included in 7 articles, and N0 and N1 esophageal

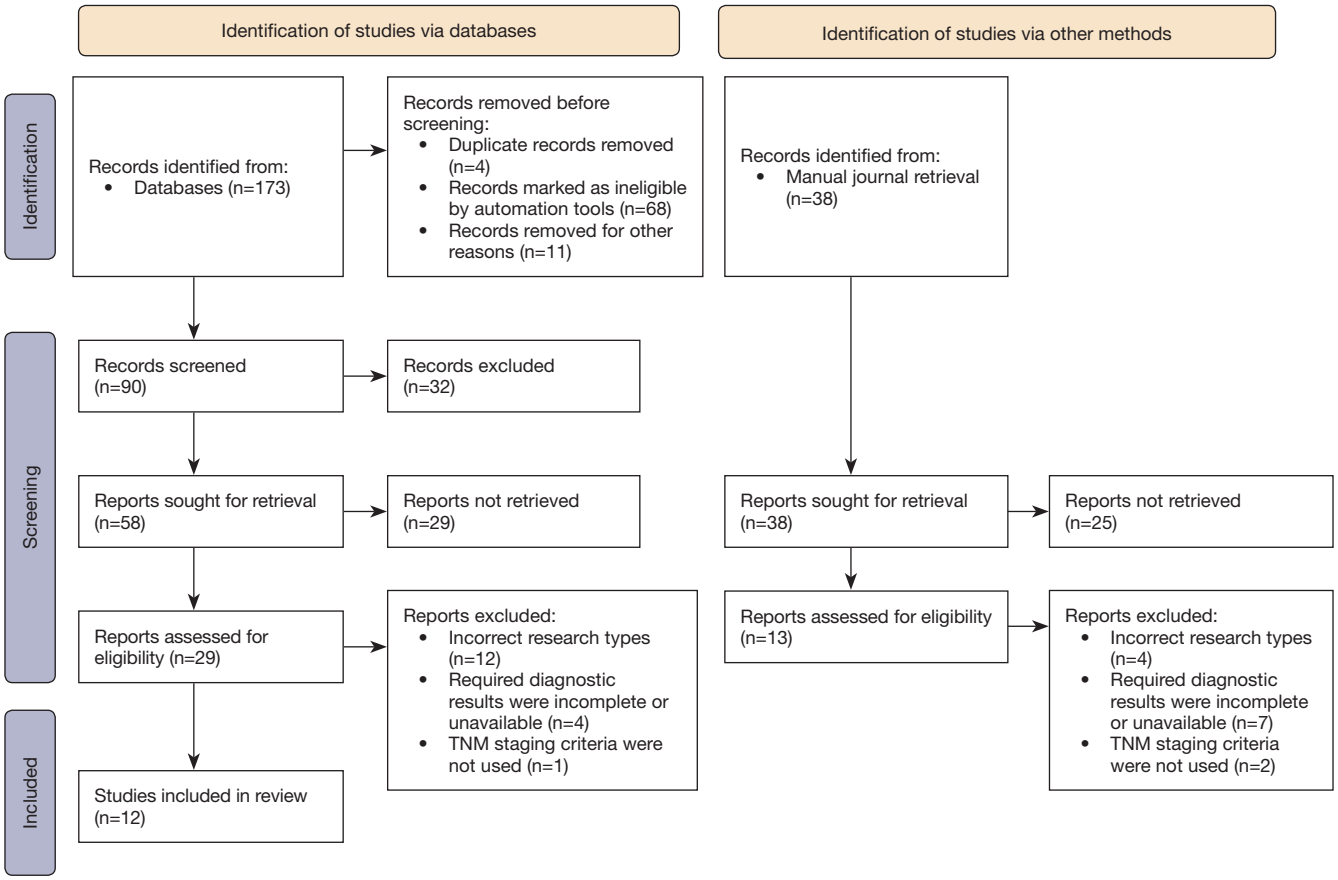

Figure 1 Article retrieval process.

cancer patients were involved in 9 articles. The results of the evaluation of the quality of 12 included articles demonstrated that 8 articles were rated level A (66.66%), 2 articles were rated level B (16.67%), and 2 articles were rated level C (16.67%). *Table 1* shows the basic features of the included articles. *Figure 2* displays the evaluation of the risk bias of the references drawn with Rev Man 5.3. *Figure 3* illustrates the summary of the risk bias of references.

Evaluation results of heterogeneity

The heterogeneity of the diagnosis of each stage using EUS in the included articles was evaluated. There was heterogeneity in the sensitivity and specificity among each article (I^2=88.55%, 75.44%). In terms of the heterogeneity results of the diagnosis of T2 stage, there was heterogeneity in the sensitivity and specificity among each article (I^2=68.39%, 70.07%). The heterogeneity results of the diagnosis of T3 stage showed that there was heterogeneity in the sensitivity and specificity among each article (I^2=76.79%, 90.24%). The heterogeneity results of the diagnosis of T4 stage indicated that there was little heterogeneity in the sensitivity and specificity among each article (I^2=35.15%, 49.78%). The heterogeneity results of the diagnosis of N0 stage revealed that there was little heterogeneity in the sensitivity and specificity among each article (I^2=59.40%, 45.87%). The heterogeneity results of the diagnosis of N1 stage demonstrated that there was heterogeneity in the sensitivity and specificity among each article (I^2=47.54%, 62.07%). There was heterogeneity among the diagnostic data of EUS for each stage, and it needed to be summarized and analyzed by random effect model and fitted with summary receiver operating characteristic (SROC) curve.

Meta-analysis of diagnosis of T1 stage using EUS

In the 12 included articles (31-42), the diagnostic results

Table 1 Basic features of the included articles

Author	Publication year	Total number of patients	Clinical stages of patients with esophageal cancer	Diagnostic mode
Bohle (31)	2016	48	T1–T3	EUS
Bowrey (32)	1999	17	T1–T3, N0–N1	EUS
DeWitt (33)	2005	102	T1–T4, N0–N1	EUS
Griffin (34)	2012	73	T1–T4, N0–N1	EUS
Heinzow (35)	2013	45	T1–T4, N0–N1	EUS
Isenberg (36)	1998	23	T1–T4	EUS
Kalha (37)	2004	83	T1–T4, N0–N1	EUS
Meister (38)	2013	143	T1–T4, N0–N1	EUS
Misra (39)	2012	110	T1–T4, N0–N1	EUS
Schneider (40)	2008	80	T1–T3	EUS
Willis (41)	2002	41	T1–T3, N0–N1	EUS
Zuccaro (42)	1999	59	T1–T3, N0–N1	EUS

EUS, endoscopic ultrasound.

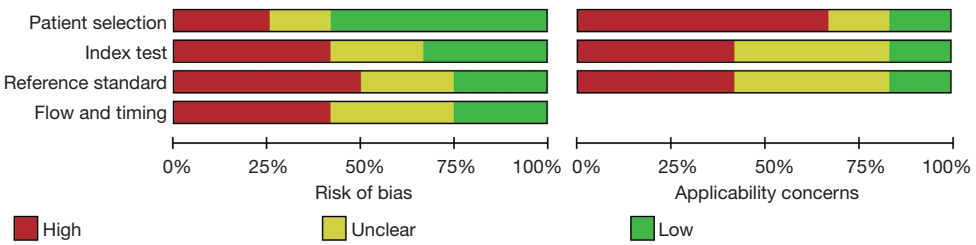

Figure 2 Risk bias evaluation diagram of included articles.

of T1 stage using EUS in diagnostic experiments were analyzed. *Figure 4* is a forest plot showing the sensitivity and specificity of individual studies and summary studies at T1 stage. Furthermore, heterogeneity test was carried out for the sensitivity of the diagnosis of T1 stage in the 12 included articles, and the results showed that Q=96.06, degree of freedom (df) =11.00, I^2=88.55%, and P=0.00, which indicated that there was heterogeneity among each research group. Furthermore, the combined sensitivity was 0.16 with a 95% CI was 0.05–0.39. The lowest sensitivity was 0.00 and 95% CI was 0.00–0.37. The highest sensitivity reached 1.00 and 95% CI was 0.03–1.00. In addition, heterogeneity test was conducted for the specificity of the diagnosis of T1 stage in the 12 included articles. The results revealed that Q=44.79, df =11.00, I^2=75.44%, and P=0.00, which suggested that there was heterogeneity among each research group. The combined specificity was 0.99 and 95% CI was 0.94–1.00. The lowest specificity was 0.82 and 95% CI was 0.60–0.95. The highest specificity was 1.00 and 95% CI was 0.96–1.00. *Figure 5* was SROC curve of T1 staging diagnosis. If the SROC was closer to the upper left corner of the image, the area under the SROC curve became larger with higher diagnostic accuracy. The results of T1 staging diagnosis showed that the proportion of false negatives and false positives was low, and the diagnostic accuracy was high.

Meta-analysis of diagnosis of T2 stage using EUS

In the 12 included articles, the diagnostic results of T2 stage using EUS in diagnostic experiments were analyzed. *Figure 6* is a forest plot showing the sensitivity and specificity of individual studies and summary studies at T2 stage. A heterogeneity test was conducted for the sensitivity of T2 staging diagnosis in the 12 included articles. The results

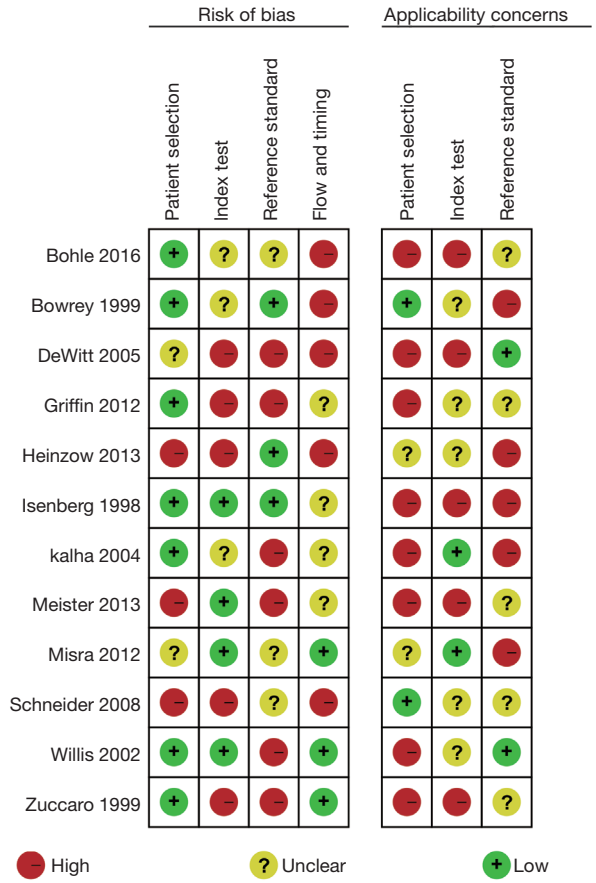

Figure 3 Risk bias evaluation and summary diagram of included articles. "+" referred to low risk, "–" represented high risk, and "?" denoted unclear.

demonstrated that Q=34.80, df =11.00, I^2=68.39%, and P=0.00, which showed that there was heterogeneity among each research group. The combined sensitivity was 0.34 and 95% CI was 0.20–0.52. The lowest sensitivity was 0.07 and 95% CI was 0.01–0.24. The highest sensitivity was 1.00 and 95% CI was 0.63–1.00. In addition, heterogeneity test was performed on the specificity of T2 staging diagnosis in the 12 included articles. The results showed that Q=36.75, df =11.00, I^2=70.07%, and P=0.00, which demonstrated that there was heterogeneity among each research group. The combined specificity was 0.80 and 95% CI was 0.74–0.85. The lowest specificity was 0.63 and 95% CI was 0.50–0.74. The highest specificity was 1.00 and 95% CI was 0.81–1.00. *Figure 7* displays the SROC curve of T2 staging diagnosis. If the SROC curve was closer to the upper left corner of the image, the area under the SROC curve became larger with higher diagnostic accuracy. The results of T2 staging diagnosis indicated that the proportion of false negatives and false positives was high with low diagnostic accuracy.

Meta-analysis of diagnosis of T3 stage using EUS

In the 12 included articles, the diagnostic results of T3 stage using EUS in diagnostic experiments were analyzed. *Figure 8* is a forest plot showing the sensitivity and specificity of individual studies and summary studies at T3 stage. A heterogeneity test was conducted for the sensitivity of T3 staging diagnosis in the 12 included articles. The results showed that Q=47.39, df =11.00, I^2=76.79%, and P=0.00, which indicated that there was heterogeneity among each research group. The combined sensitivity was 0.78 and 95% CI was 0.63–0.88. The lowest sensitivity was 0.38 and 95% CI was 0.14–0.68. The highest sensitivity was 1.00 and 95% CI was 0.85–1.00. Furthermore, heterogeneity test was conducted for the specificity of T3 staging diagnosis in the 12 included articles. The results revealed that Q=112.69, df =11.00, I^2=90.24%, and P=0.00, which demonstrated that there was high heterogeneity among each research group. The combined specificity was 0.52 and 95% CI was 0.36–0.68. The lowest specificity was 0.17 and 95% CI was 0.09–0.28. The highest specificity was 1.00 and 95% CI was 0.59–1.00. *Figure 9* presents the SROC curve of T3 staging diagnosis. If the SROC curve was closer to the upper left corner of the image, the area under the SROC curve became larger with higher diagnostic accuracy. The results of T3 staging diagnosis showed that the proportion of false negatives and false positives was high with low diagnostic accuracy.

Meta-analysis of diagnosis of T4 stage using EUS

In 7 included articles (33-39), the diagnostic results of T4 stage using EUS in diagnostic experiments were analyzed. *Figure 10* is a forest plot showing the sensitivity and specificity of individual studies and summary studies at T4 stage. A heterogeneity test was conducted for the sensitivity of T4 staging diagnosis in 7 included articles. The results revealed that Q=9.25, df =6.00, I^2=35.15%, and P=0.16, which demonstrated that there was low heterogeneity among each research group. The combined sensitivity was 0.16 and 95% CI was 0.04–0.50. The lowest sensitivity was 0.00 and 95% CI was 0.00–0.52. The highest sensitivity was 1.00 and 95% CI was 0.03–1.00. In addition, heterogeneity test was conducted for the specificity of T4 staging diagnosis in 7 included articles. The results indicated that Q=11.95,

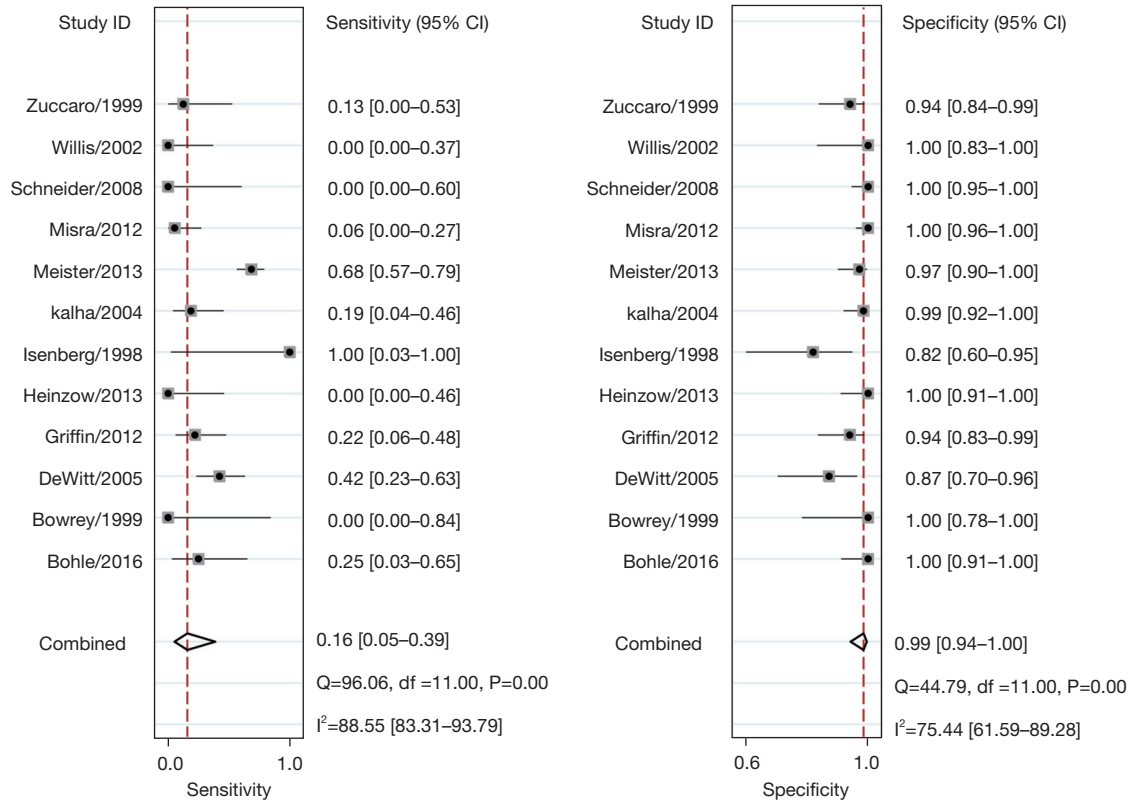

Figure 4 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of T1 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

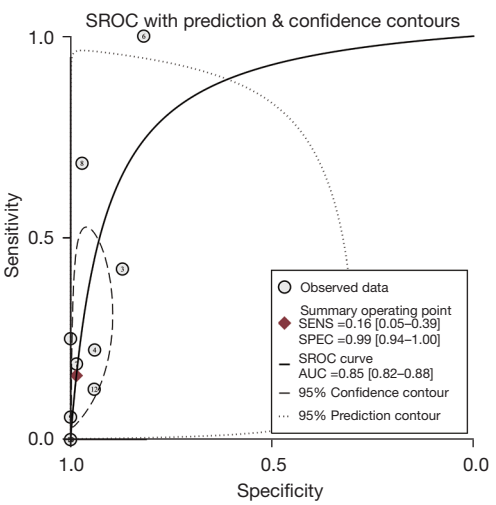

Figure 5 SROC curve of the diagnosis of T1 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

df =6.00, I^2=49.78%, and P=0.06, which demonstrated that there was heterogeneity among each research group. The combined specificity was 0.98 and 95% CI was 0.95–0.99. The lowest specificity was 0.91 and 95% CI was 0.78–0.97. The highest specificity was 1.00 and 95% CI was 0.97–1.00. *Figure 11* displays the SROC curve of T4 staging diagnosis. If the SROC curve was closer to the upper left corner of the images, the area under the SROC curve became larger with higher diagnostic accuracy. The results of T4 staging diagnosis showed that the proportion of false negatives and false positives was low with high diagnostic accuracy.

Meta-analysis of diagnosis of N0 stage using EUS

In 9 included articles (32-35,37-39,41,42), the diagnostic results of N0 stage using EUS in diagnostic experiments were analyzed. *Figure 12* is a forest plot showing the sensitivity and specificity of individual studies and summary

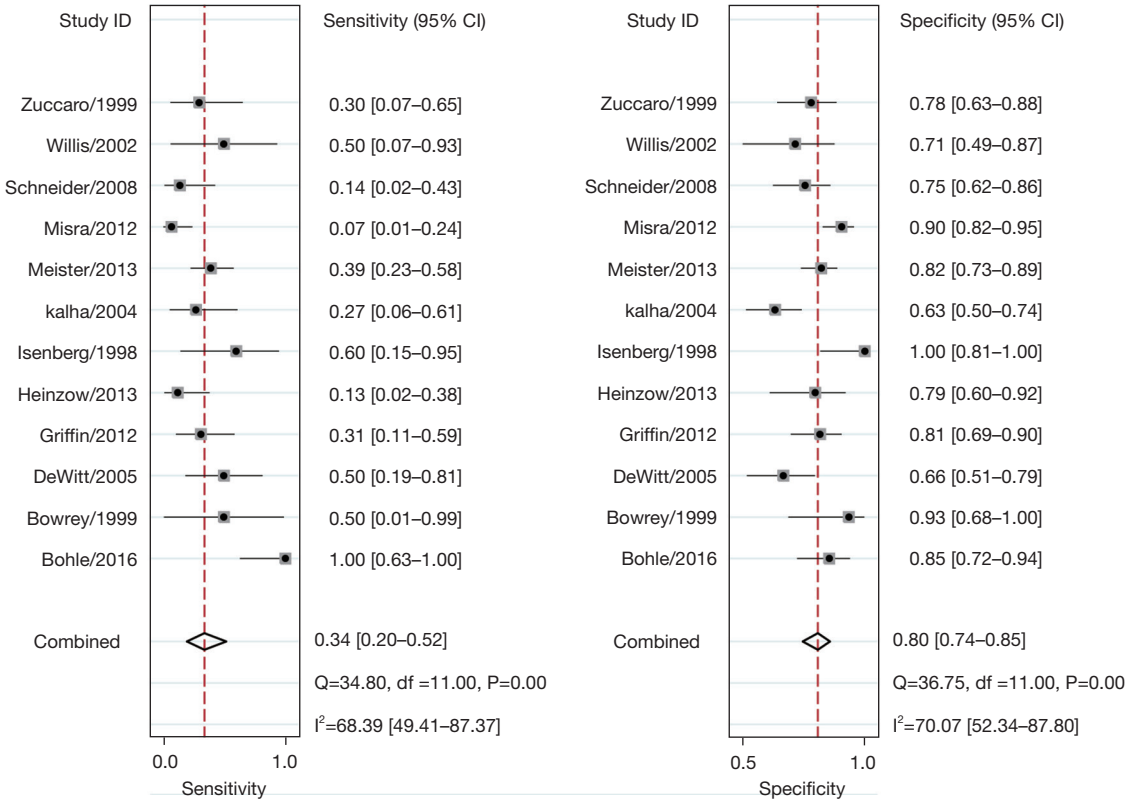

Figure 6 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of T2 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

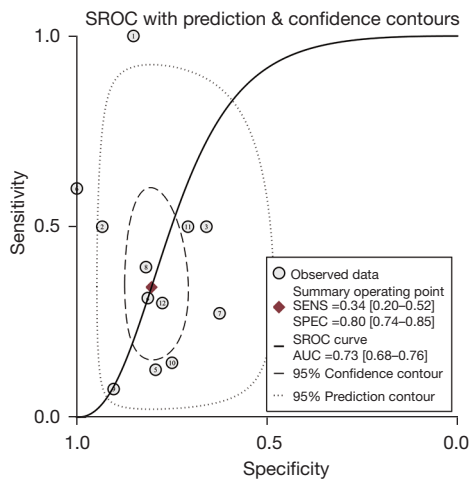

Figure 7 SROC curve of the diagnosis of T2 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

studies at N0 stage. A heterogeneity test was conducted for the sensitivity of N0 staging diagnosis in 9 included articles. The results demonstrated that Q=19.70, df =8.00, I^2=59.40%, and P=0.01, which showed that there was heterogeneity among each research group. The combined sensitivity was 0.62 and 95% CI was 0.53–0.71. The lowest sensitivity was 0.45 and 95% CI was 0.17–0.77. The highest sensitivity was 1.00 and 95% CI was 0.03–1.00. In addition, heterogeneity test was implemented for the specificity of N0 staging diagnosis in 9 included articles. The results showed that Q=14.78, df =8.00, I^2=45.87%, and P=0.06, which revealed that there was heterogeneity among each research group. The combined specificity was 0.65 and 95% CI was 0.58–0.71. The lowest specificity was 0.38 and 95% CI was 0.18–0.62. The highest specificity was 0.83 and 95% CI was 0.36–1.00. *Figure 13* presents the SROC curve of N0 staging diagnosis. If the SROC curve was closer to the upper left corner of the images, the area under the SROC

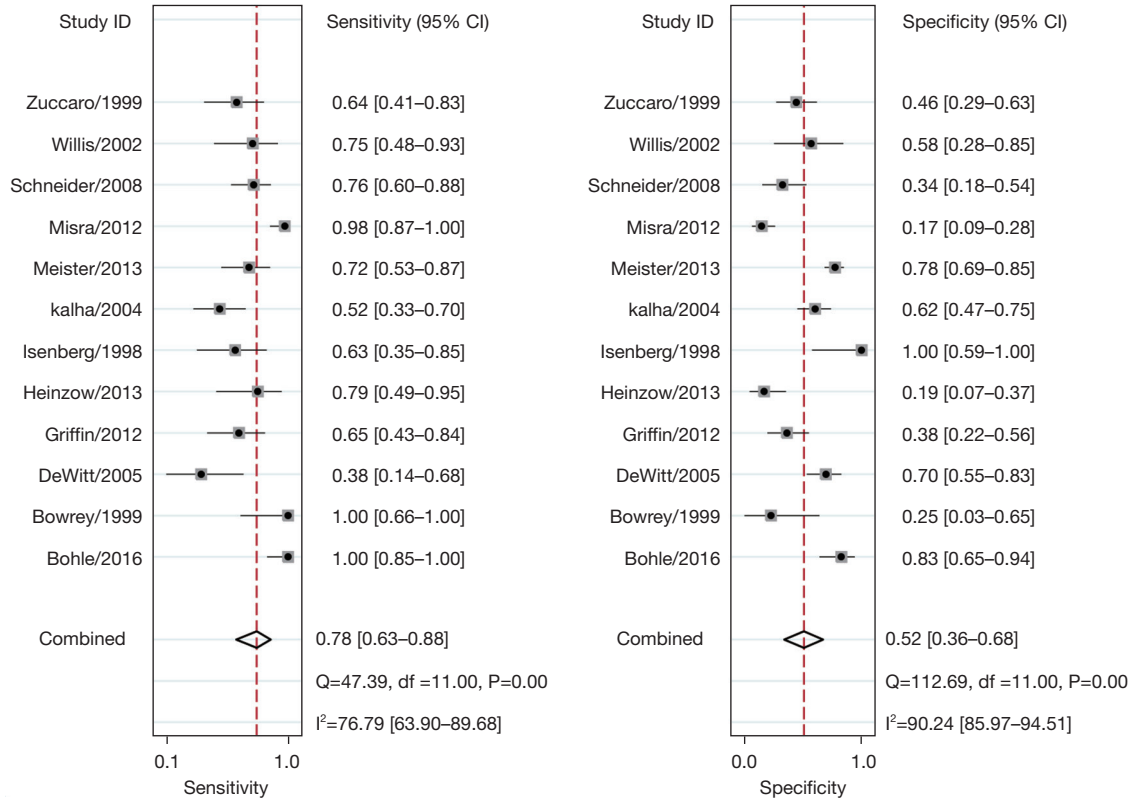

Figure 8 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of T3 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

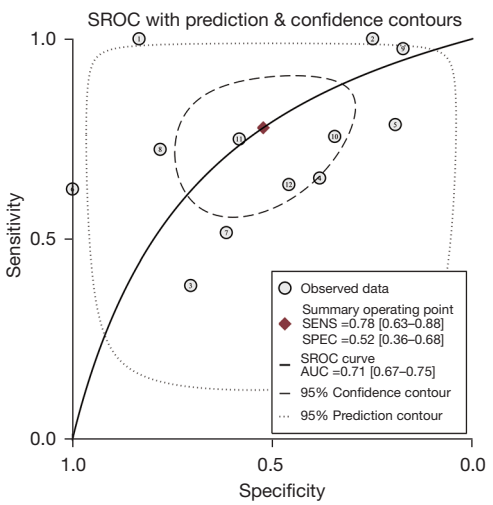

Figure 9 SROC curve of the diagnosis of T3 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

curve became larger with higher diagnostic accuracy. The results of N0 staging diagnosis showed that the proportion of false negatives and false positives was high with low diagnostic accuracy.

Meta-analysis of diagnosis of N1 stage using EUS

In 9 included articles, the diagnostic results of N1 stage using EUS in diagnostic experiments were analyzed. *Figure 14* is a forest plot showing the sensitivity and specificity of individual studies and summary studies at N1 stage. Heterogeneity test was carried out for the sensitivity of N1 staging diagnosis in 9 included articles. The results showed that Q=15.25, df =8.00, I^2=47.54%, and P=0.05, which demonstrated that there was heterogeneity among each research group. The combined sensitivity was 0.65 and 95% CI was 0.58–0.72. The lowest sensitivity was 0.38 and 95% CI was 0.18–0.62. The highest sensitivity was 0.83 and

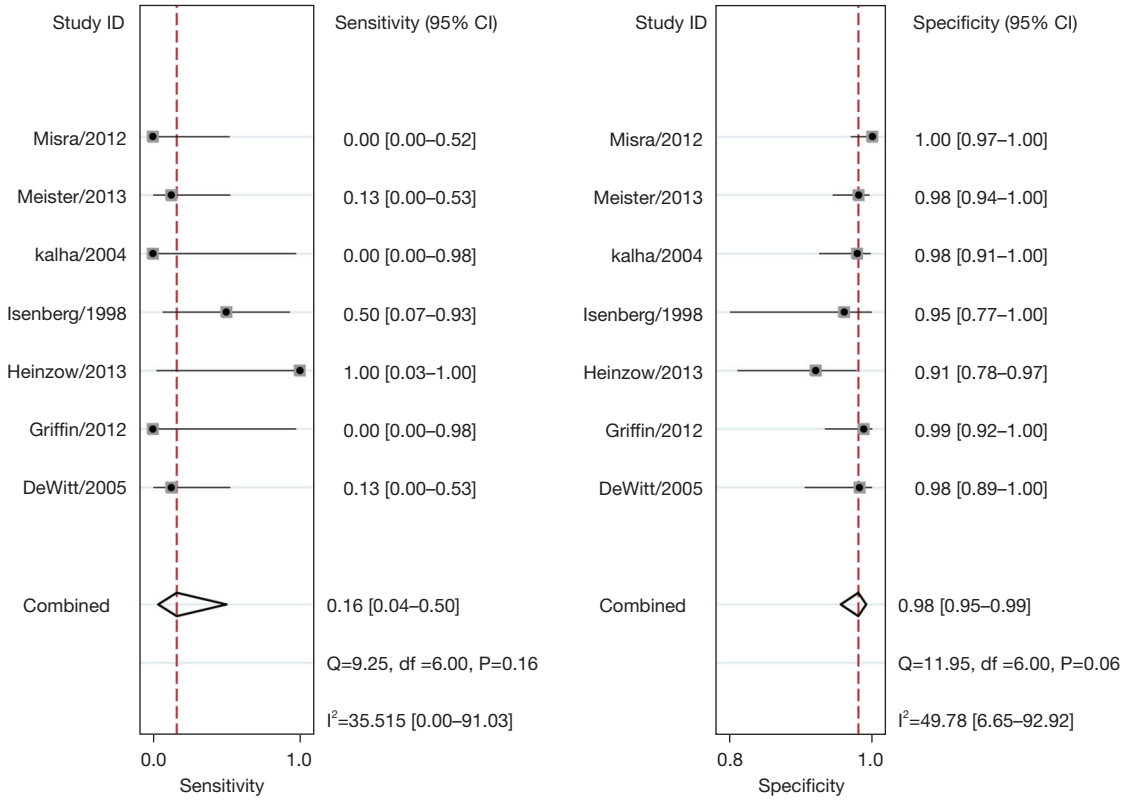

Figure 10 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of T4 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

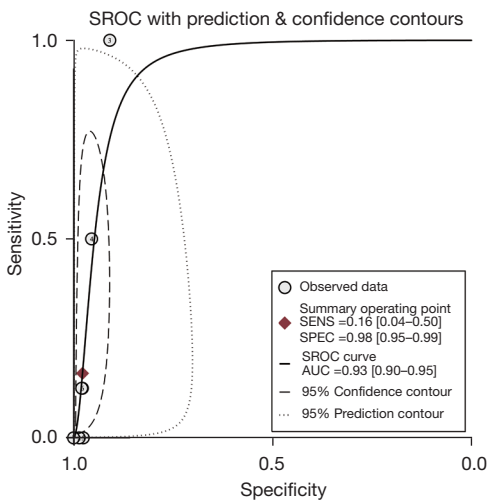

Figure 11 SROC curve of the diagnosis of T4 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

95% CI was 0.36–1.00. In addition, heterogeneity test was implemented for the specificity of N1 staging diagnosis in 9 included articles. The results indicated that Q=21.09, df =8.00, I^2=62.07%, and P=0.01, which showed that there was heterogeneity among each research group. The combined specificity was 0.63 and 95% CI was 0.54–0.72. The lowest specificity was 0.45 and 95% CI was 0.17–0.77. The highest specificity was 1.00 and 95% CI was 0.03–1.00. *Figure 15* displays the SROC curve of N1 staging diagnosis. If the SROC curve was closer to the upper left corner of the image, the area under the SROC curve became larger with higher diagnostic accuracy. The results of N1 staging diagnosis demonstrated that the proportion of false negatives and false positives was high with low diagnostic accuracy.

Sensitivity analysis

Sensitivity analysis was carried out by changing the analysis

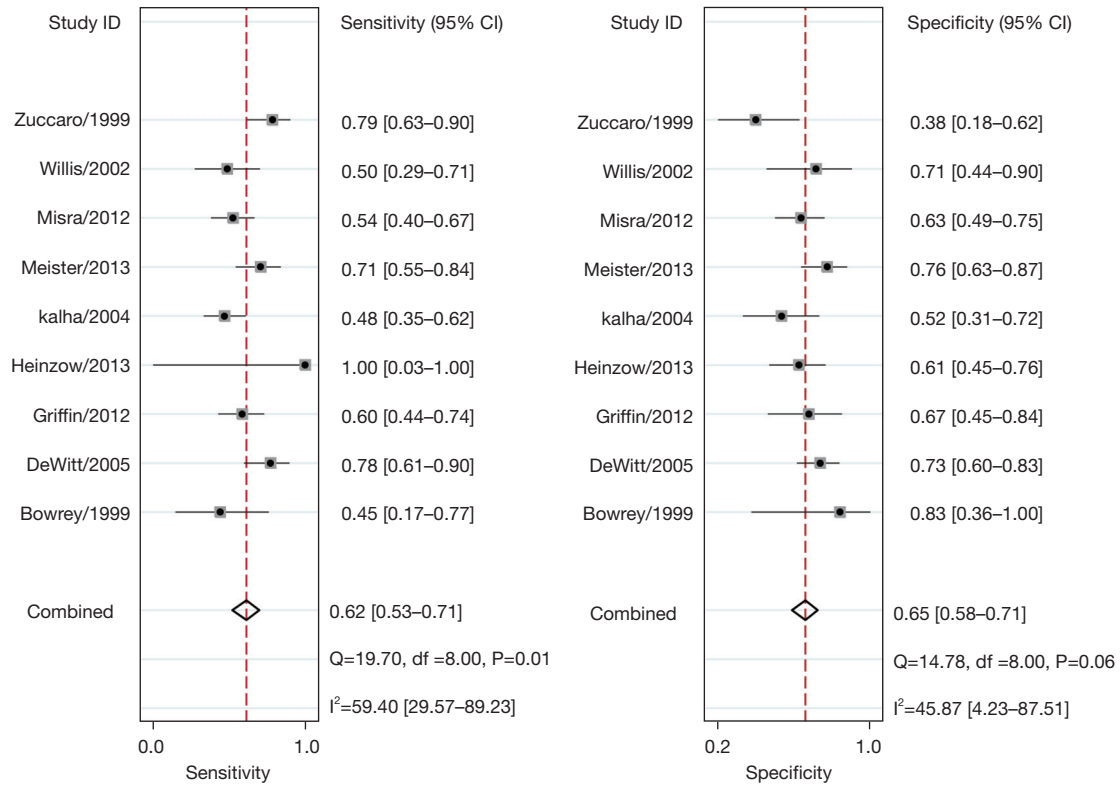

Figure 12 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of N0 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

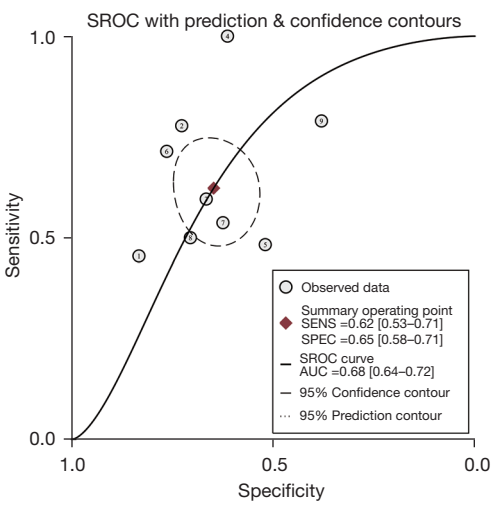

Figure 13 SROC curve of the diagnosis of N0 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

model. The results of the meta-analysis and the summary results of the application of different analysis models showed no obvious changes, which indicated that the included articles showed good stability.

Discussion

Esophageal cancer is a common malignant tumor characterized by the invasion of peripheral tissues and metastasis. In recent years, surgical operational and medical technical levels have constantly improved, but the postoperative 5-year survival rate of patients with esophageal cancer is still extremely low. Simple surgical treatment cannot meet the clinical needs of patients with esophageal cancer (43,44). To further enhance the long-term survival rate of patients with esophageal cancer, the implementation of neoadjuvant chemotherapy before surgery attracts extensive attention from medical staff and

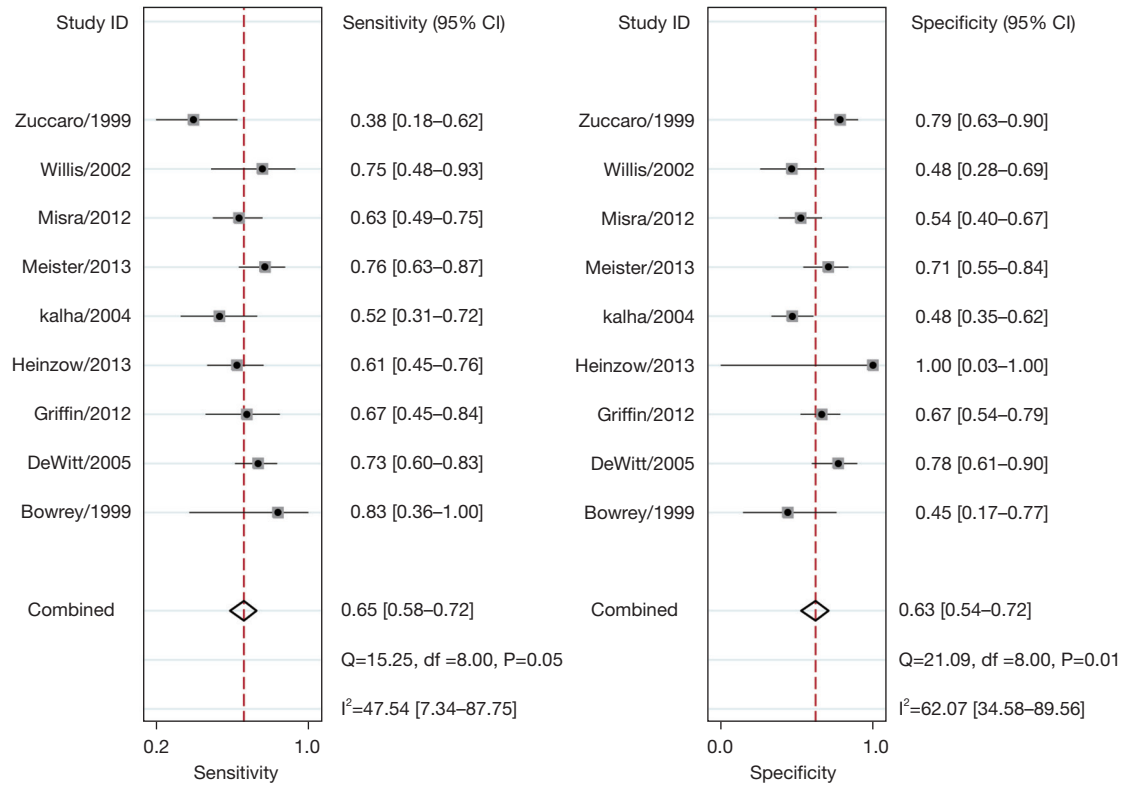

Figure 14 Forest plot of sensitivity and specificity of individual study and summary study on the diagnosis of N1 stage using EUS. CI, confidence interval; df, degree of freedom; EUS, endoscopic ultrasound.

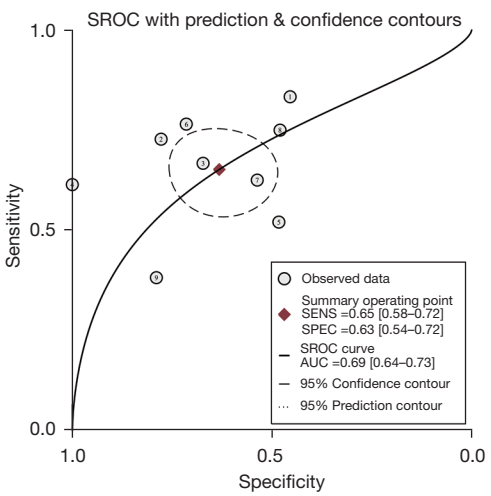

Figure 15 SROC curve of the diagnosis of N1 stage using EUS. SROC, summary receiver operating characteristic; AUC, area under curve; SENS, sensitivity; SPEC, specificity; EUS, endoscopic ultrasound.

it shows good therapeutic effects (45). Multiple studies show that neoadjuvant chemotherapy can effectively improve the long-term survival rate of patients with esophageal cancer and alleviate patients' clinical symptoms (46,47). Nonetheless, neoadjuvant chemotherapy shows some limitations at present. Clinically, there no effective assessment method for the therapeutic effects of neoadjuvant chemotherapy. Furthermore, patients cannot be staged accurately, and the misjudgment of the staging for patients with esophageal cancer after neoadjuvant chemotherapy will affect the direction of subsequent treatment for patients (48).

EUS is mainly to observe and evaluate the depth of cancer invasion into esophageal wall, the extent of invasion into mediastinum and swollen lymph nodes in mediastinum to complete the diagnosis and staging of patients (49). Furthermore, EUS can measure the diameter and cross-sectional area of the esophageal wall and gastric wall

by ultrasound. Relevant study (50) demonstrates that the percentage of the reduction in the maximum cross-sectional area of EUS is closely related to the efficacy of neoadjuvant therapy. If the maximum cross-sectional area of EUS is reduced by over 50%, neoadjuvant chemotherapy is effective for tumors. Clinically, the studies on the adoption of EUS to assess TNM staging after neoadjuvant chemotherapy for patients with esophageal cancer flourish. Among each study, the accuracy of determining the depth of esophageal cancer infiltration using EUS was different. According to a study (51), the accurate judgment of clinical staging using EUS can improve the clinical therapeutic effects on about three-quarters of patients. Furthermore, over half of all patients offer valid information to subsequent treatment plans after EUS examination, which reduces the risks that patients face and reduces treatment costs. Current domestic and foreign articles on the evaluation of the efficacy of neoadjuvant chemotherapy on esophageal cancer using EUS were included. A meta-analysis system was used to assess the diagnostic capacity of esophageal cancer staging after neoadjuvant chemotherapy using EUS to evaluate the references values of EUS in analyzing and diagnosing esophageal cancer, which provided a theoretical reference and basis for the assessment of therapeutic effects of neoadjuvant chemotherapy on esophageal cancer.

In the meta-analysis, the diagnostic accuracy of the clinical staging after neoadjuvant chemotherapy for patients with esophageal cancer using EUS was estimated and evaluated. A total of 12 articles were included and the diagnosis of T1-T4 sensitivity was assessed with a heterogeneity test. The results were as follows—T1: Q=96.06, df =11.00, I^2=88.55%, and P=0.00; T2: Q=34.80, df =11.00, I^2=68.39%, and P=0.00; T3: Q=47.39, df =11.00, I^2=76.79%, and P=0.00; T4: Q=9.25, df =6.00, I^2=35.15%, and P=0.16. The results demonstrated that there was heterogeneity among each research group. The combined sensitivity was 0.16 with a 95% CI of 0.05–0.39, 0.34 with a 95% CI of 0.20–0.52, 0.78 with a 95% CI of 0.63–0.88, and 0.16 with a 95% CI of 0.04–0.50. Furthermore, the specificity of T staging diagnosis using EUS in the 12 included articles was assessed with a heterogeneity test. T1 to T4 were Q=44.79, df =11.00, I^2=75.44%, and P=0.00; Q=36.75, df =11.00, I^2=70.07%, and P=0.00; Q=111.69, df =11.00, I^2=90.24%, and P=0.00; and Q=9.25, df =6.00, I^2=35.15%, and P=0.16. The results showed that there was heterogeneity among each research group. The combined specificities were 0.99 with a 95% CI of 0.94–1.00, 0.80 with a 95% CI of 0.74–0.85, 0.52 with a 95% CI of 0.36–0.68, and 0.98 with a 95% CI of 0.95–0.99. In addition, the sensitivity of N0 and N1 diagnosis using EUS was assessed with a heterogeneity test. The results showed that Q=19.70, df =8.00, I^2=59.40%, P=0.01 and Q=15.25, df =8.00, I^2=47.54%, P=0.05, which indicated that there was no heterogeneity among each research group. The combined sensitivities were 0.62 with a 95% CI of 0.53–0.71 and 0.65 with a 95% CI of 0.58–0.72. Furthermore, the specificity of N0 and N1 diagnosis using EUS in 9 included articles was assessed with a heterogeneity test, which showed Q=14.78, df =8.00, I^2=45.87%, and P=0.06; and Q=21.09, df =8.00, I^2=62.07%, and P=0.01. The results demonstrated that there was heterogeneity among each research group. The combined specificity was 0.65 with a 95% CI of 0.58–0.71 and 0.63 with a 95% CI of 0.54–0.72. In addition, the area under the SROC curve reflected the diagnostic values diagnostic methods possessed. A larger area under curve meant higher diagnostic values. The areas under curves of T1 and T4 diagnosed using EUS were 0.85 and 0.93, respectively, which indicated that they showed high diagnostic values. In addition, the sensitivity of TNM staging was generally low and the specificity was high, which was consistent with the study conducted by Sun *et al.* (52). The low sensitivity might be related to local fibrosis and inflammation in patients' esophageal tissues after neoadjuvant chemotherapy, which could reduce tumor size. However, patients' esophageal structure cannot return to normal. As a result, it was difficult to assess the depth of tumors accurately.

The diagnostic capacity of the clinical staging for patients with esophageal cancer after neoadjuvant chemotherapy using EUS was synthesized and assessed in the meta-analysis. The meta-analysis provided evidence-based suggestions on clinical practical guidance. In clinical studies, EUS could be used to accurately assess the clinical TNM staging of patients with esophageal cancer, which can offer more accurate reference for subsequent treatment.

Conclusions

The articles related to the diagnosis and assessment of the clinical staging for patients with esophageal cancer after neoadjuvant chemotherapy using EUS were selected and included in the meta-analysis. The meta-analysis investigated the accuracy of the evaluation of the clinical effects of neoadjuvant chemotherapy on patients with esophageal cancer using EUS. The results of the meta-analysis confirmed that the sensitivity of determining TNM

clinical staging of patients with esophageal cancer using EUS was poor, while its specificity was good. Furthermore, EUS showed high accuracy in diagnosing patients at T1 and T4 stages. The significant heterogeneity among articles might be related to the fact that there was no uniform time criterion between neoadjuvant chemotherapy and EUS examination. Furthermore, the differences in sample size and design in articles also caused heterogeneity. A uniform criterion needs to be formulated. In addition, more samples and high-quality articles should be analyzed to provide a more accurate and effective basis for clinical practice.

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Footnote

Reporting Checklist: The authors have completed the PRISMA-DTA reporting checklist. Available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-437/rc

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jgo.amegroups.com/article/view/10.21037/jgo-22-437/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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