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Comparative Diagnostic Efficacy of Endoscopic Modalities for Gastric Neoplasms and Precancerous Lesions: A Network Meta-Analysis

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1. Abstract

1.1. Background

The comparative diagnostic efficacy of different endoscopic modalities for gastric precancerous lesions, including atrophy, intestinal metaplasia, and intraepithelial neoplasia, as well as gastric neoplasms, has not been conclusively established.

1.2. AIM

This network meta-analysis (NMA) evaluated and ranked the relative diagnostic performance of available endoscopic modalities.

1.2. METHODS

A systematic literature search was conducted in MEDLINE, EMBASE, and the Cochrane Library from database inception to December 2025. Two reviewers independently screened the studies, extracted data, and assessed the risk of bias. A Bayesian NMA based on an analysis of variance model was performed to estimate pooled sensitivity, specificity, and diagnostic odds ratios for each modality. The modalities were subsequently ranked using the superiority index.

1.3. Results

A total of 11,293 patients from 22 studies were included. For gastric atrophy, confocal laser endomicroscopy (CLE) demonstrated the highest sensitivity (0.77, 95% CI: 0.32–0.98) and ranked first according to the superiority index, while white light endoscopy (WLE) exhibited the highest specificity (0.92, 95% CI: 0.78-0.97). For intestinal metaplasia, linked colour imaging (LCI) and CLE showed superior diagnostic performance, with CLE exhibiting the highest sensitivity (0.91, 95% CI: 0.79–0.97). For high-grade intraepithelial neoplasia and gastric neoplasms, CLE ranked first with the highest specificity (0.97, 95% CI: 0.91–0.99), whereas blue laser imaging (BLI) demonstrated the highest sensitivity (0.92, 95% CI: 0.81–0.98). Although narrow band imaging (NBI) was not top-ranked, its overall high efficacy indicates considerable potential. Autofluorescence endoscopy and WLE consistently showed inferior diagnostic performance across all lesion types.

1.4. Conclusion

This NMA provides a quantitative, lesion-specific hierarchy of endoscopic modalities. CLE demonstrated promising diagnostic performance, especially for atrophy and neoplasia. WLE exhibited high specificity for atrophy. Some advanced image-enhanced endoscopy techniques, particularly BLI, LCI, and NBI, also showed high diagnostic value and potential. While the overall ranking should be interpreted with caution due to varying evidence strength and limited data for certain modalities.

1.5. Core Tip

This network meta-analysis synthesized both direct and indirect evidence across a broad range of endoscopic modalities and lesion types. Confocal laser endomicroscopy ranked first for atrophy, high-grade intraepithelial neoplasia, gastric neoplasms and second for intestinal metaplasia. At the same time, some advanced image-enhanced endoscopy techniques demonstrated superior diagnostic performance compared with white light endoscopy.

2. Introduction

Gastric cancer is one of the most prevalent gastrointestinal malignancies, ranking fifth worldwide in both incidence and cancer-related mortality [1], and continues to pose a substantial public health burden. Its pathogenesis generally follows Correa's cascade, a multistep process progressing from chronic gastritis through precancerous stages-namely atrophy, intestinal metaplasia, and intraepithelial neoplasia-to invasive adenocarcinoma [2]. The prognosis of gastric cancer is highly dependent on disease stage. Patients diagnosed and treated at an early stage have a markedly higher 5-year survival rate (>70%) compared with those with advanced-stage disease (<10%) [3].

Although effective treatment substantially improves outcomes in early-stage gastric cancer, its overall impact is limited by low detection rates. In routine clinical practice without risk stratification, the detection rate of early gastric cancer (EGC) has been reported to be as low as 26.9% [4]. This low rate of early diagnosis represents a major obstacle to reducing gastric cancer–related mortality through screening. A systematic review has shown that the global uptake of endoscopic screening remains below 50%, and even among detected cases, the proportion of EGC remains suboptimal [5]. These findings suggest that low detection rates may be attributable to both insufficient screening coverage and the limitations of existing diagnostic tools. Therefore, strategies to improve early detection should address both factors, potentially by increasing screening participation and adopting more advanced endoscopic technologies.

Currently, white light endoscopy (WLE) is the cornerstone modality for the examination of gastric lesions in clinical practice [6]. However, its diagnostic performance for EGC and precancerous lesions is limited, partly because these lesions often exhibit subtle morphological and colour changes that are difficult to recognize under conventional white light, leading to missed diagnoses [7]. To overcome these limitations, a range of advanced endoscopic modalities has been developed and refined.

These advanced techniques can be broadly classified into two categories. The first category comprises image-enhanced endoscopy (IEE), which includes dye-less digital technologies such as narrow-band imaging (NBI), blue laser imaging (BLI), linked colour imaging (LCI), and texture and colour enhancement imaging (TXI). These modalities enhance mucosal surface and vascular patterns without the use of exogenous dyes. Chromoendoscopy (CE), which employs topical chemical dyes to improve mucosal contrast, is also included within this group. The second category consists of virtual histology techniques, such as confocal laser endomicroscopy (CLE) and endocytic, which enable real-time, in vivo microscopic imaging at the cellular level, approaching the resolution of conventional histopathology.

Although these advanced modalities collectively address many of the limitations associated with WLE, evidence regarding their comparative diagnostic efficacy for gastric neoplasms and precancerous lesions remains insufficient. While numerous primary studies and pairwise meta-analyses have evaluated selected techniques, a comprehensive comparison encompassing all available modalities is lacking. A network meta-analysis (NMA) represents the most appropriate methodological approach for synthesizing such evidence, as it allows for the simultaneous comparison and ranking of multiple interventions, even in the absence of direct head-to-head trials.

Accordingly, this study employed a Bayesian NMA based on an analysis of variance (ANOVA) model to synthesize and compare the diagnostic performance of various endoscopic modalities for gastric neoplasms and precancerous lesions [8]. Diagnostic sensitivity, specificity, and diagnostic odds ratios (DORs) were comprehensively evaluated. By incorporating the superiority index into the analytical framework [9], an overall ranking of diagnostic performance was generated. This study aims to provide evidence-based guidance for the selection of endoscopic modalities in clinical practice.

3. Methods

3.1. Protocol Registration

This systematic review and network meta-analysis was conducted in accordance with the PRISMA-NMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Network Meta-Analyses) guidelines [10]. The study protocol was prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration number CRD420251058198).

3.2. Information Sources and Search Strategy

A comprehensive literature search was performed in three major electronic databases: MEDLINE (via PubMed), EMBASE (via Ovid), and the Cochrane Central Register of Controlled Trials (CENTRAL), from database inception to December 2025. The search strategy was developed in collaboration with a medical librarian and incorporated both controlled vocabulary terms (e.g., Medical Subject Headings [MeSH] and Entree terms) and free-text keywords related to the main concepts of the study. The detailed search strategy is provided in the Appendix (see Supplementary Table 1. Search Strategy).

3.3. Study Selection Criteria

Study eligibility was defined according to the PICOS framework [11]: (i) Population: adult patients (≥18 years) undergoing esophagogastroduodenoscopy for screening, surveillance, or diagnostic evaluation of gastric lesions, including gastric neoplasms (both early and advanced gastric cancer) and precancerous lesions (atrophy, intestinal metaplasia, and intraepithelial neoplasia); (ii) Index tests: endoscopic modalities including WLE, NBI, LCI, BLI, TXI, Optical Enhancement (OE), autofluorescence endoscopy (AFE), endocytoscopy, and CLE; (iii) Comparator: all index tests were compared with one another, with histopathological examination of biopsy or resection specimens serving as the common reference standard; (iv) Outcomes: diagnostic performance for gastric neoplasms or precancerous lesions, with sufficient data to calculate true-positive (TP), false-positive (FP), true-negative (TN), and false-negative (FN) values; (v) Study design: diagnostic test accuracy studies, including prospective or retrospective cohort studies and diagnostic randomized controlled trials. Cross-sectional studies meeting the above criteria were also eligible. Although several modalities were listed in the search strategy, some had no eligible studies with extractable data and were not included in the final analysis.

Search results were imported into reference management software (e.g., EndNote), and duplicate records were removed. Using predefined screening forms in Covidence or Rayyan, two reviewers independently screened titles and abstracts, followed by full-text assessment of potentially eligible studies. Discrepancies were resolved through discussion.

3.4. Outcomes

The primary outcomes were measures of diagnostic efficacy for gastric neoplasms and precancerous lesions, including sensitivity, specificity, DORs, superiority index, relative sensitivity, and relative specificity. In addition, data on mean procedural time and adverse events were extracted (see Supplementary Table 5).

Supplementary Table 1: Search strategy (using Pubmed as an example).

	Search strategy
#1	"Stomach Neoplasms"[MeSH Terms] OR "Adenocarcinoma"[MeSH Terms] OR "Precancerous Conditions"[MeSH Terms] OR ("gastric cancer"[Title/Abstract] OR "early gastric cancer"[Title/Abstract] OR "advanced gastric cancer"[Title/Abstract] OR "gastric neoplas*"[Title/Abstract] OR "gastric tumor*"[Title/Abstract] OR "gastric carcinoma"[Title/Abstract] OR "gastric malignancy"[Title/Abstract] OR "EGC"[Title/Abstract] OR "AGC"[Title/Abstract]
#2	"Gastric Dysplasia"[Title/Abstract] OR "Atrophic Gastritis"[Title/Abstract] OR "Intestinal Metaplasia"[Title/Abstract] OR "Gastric Intraepithelial Neoplasia"[Title/Abstract] OR "gastric precancer*"[Title/Abstract] OR "gastric atrophy"[Title/Abstract] OR "gastric metaplas*"[Title/Abstract] OR "GIN"[Title/Abstract] OR "OLGA staging"[Title/Abstract] OR "OLGIM staging"[Title/Abstract]
#3	"endoscopy, digestive system"[MeSH Terms] OR "white light endoscop*"[Title/Abstract] OR "WLE"[Title/Abstract] OR "standard endoscop*"[Title/Abstract] OR "high definition endoscop*"[Title/Abstract] OR "hd endoscop*"[Title/Abstract]
#4	"Narrow Band Imaging"[MeSH Terms] OR "NBI"[Title/Abstract] OR "narrow band imag*"[Title/Abstract]
#5	"Multimodal Imaging"[MeSH Terms] OR "LCI"[Title/Abstract] OR "linked color imag*"[Title/Abstract]
#6	"BLI"[Title/Abstract] OR "blue laser imag*"[Title/Abstract]
#7	"microscopy, confocal"[MeSH Terms] OR "endocytoscop*"[Title/Abstract]
#8	"CLE"[Title/Abstract] OR "confocal laser endomicroscop*"[Title/Abstract] OR "pCLE"[Title/Abstract] OR "Cellvizio"[Title/Abstract]
#9	"case reports"[Title] OR "Review"[Title] OR "Guideline"[Title] OR "Comment"[Title] OR "case reports"[Publication Type] OR "Review"[Publication Type] OR "practice guideline"[Publication Type] OR "Comment"[Publication Type]
#10	"clinical trial"[Publication Type]
#11	((#1 OR #2) AND (#3 OR #4 OR #5 OR #6 OR #7 OR #8)) NOT #9 AND #10

Supplementary Table 2: Available data for LGIN.

Study	**TP**	**FP**	**FN**	**TN**	**Test**	**Sensitivity**	**Specificity**
Li 2014	11	0	1	55	CLE	0.92(0.62,0.99)	1.00(0.94,1.00)
Zuo 2017	14	2	2	96	CLE	0.88(0.62,0.98)	0.98(0.93,0.99)
Yang 2019	4	5	4	236	WLE	0.50(0.16,0.84)	0.98(0.95,0.99)
Yang 2019	4	5	4	236	BLI	0.50(0.16,0.84)	0.98(0.95,0.99)
Yang 2019	4	4	4	237	BLI	0.50(0.16,0.84)	0.98(0.96,0.99)

(TP, true-positive; FP, false-positive; FN, false-negative; TN, true-negative; WLE, white light endoscopy; CLE, confocal laser endomicroscopy; BLI, blue laser imaging).

Supplementary Table 3: Study heterogeneity, including between-study variance (τ^2), intra-class correlation coefficient (ICC), and I^2 statistic.

		τ^2	**ICC**	I^2
Atrophy	Sensitivity	2.07[0.01,20.03]	0.42[0.00,0.94]	41.9%
	Specificity	2.58[0.03,20.45]	0.87[0.01,1.00]	86.7%
IM	Sensitivity	0.08[0.01,0.78]	0.15[0.00,0.68]	14.6%
	Specificity	1.62[0.08,6.06]	0.79[0.05,0.98]	79.4%
HGIN/GN	Sensitivity	0.24[0.01,1.83]	0.63[0.00,1.00]	62.7%
	Specificity	0.40[0.01,3.23]	0.44[0.00,0.94]	43.5%

(IM, intestinal metaplasia; HGIN, high-grade intraepithelial neoplasia; GN, gastric neoplasms).

Supplementary Table 4: Local inconsistency.

Sensitivity	p-value
IM	
WLE vs. CE	0.72
CE vs. OE	0.39
WLE vs. OE	0.18
HGIN/GN	
WLE vs. NBI	0.42
WLE vs. CLE	0.4
NBI vs. CLE	0.42

Specificity	p-value
IM	
WLE vs. CE	0.99
CE vs. OE	0.9
WLE vs. OE	0.55
HGIN/GN	
WLE vs. NBI	0.38
WLE vs. CLE	0.38
NBI vs. CLE	0.37

(IM, intestinal metaplasia; HGIN, high-grade intraepithelial neoplasia; GN, gastric neoplasms; WLE, white light endoscopy; NBI, narrow-band imaging; CLE, confocal laser endomicroscopy; CE, chromoendoscopy; OE, optical enhancement).

.**Supplementary Table 5**: Procedural time

Study	Endoscopy	Mean time/Media time (min)
Ezoe 2011	WLE	0.35
	NBI	0.92
So 2013	WLE	9
	NBI	14
Xirouchakis 2013	WLE	3.3
	NBI	4
Li 2014	WLE	18
	CLE	19
Song 2021	OE	1.07
	CE	2.52
Yoshida 2021	WLE	3.88
	NBI	4.23
Ming 2022	WLE	4.57
	LCI	4.28
Kadota 2024	WLE	4.04
	NBI	4.45
	TXI	4.29
Wan 2025	WLE	10.14
	OE	14.61

(WLE, white light endoscopy; NBI, narrow-band imaging; CLE, confocal laser endomicroscopy; CE, chromoendoscopy; LCI, linked color imaging; OE, optical enhancement; TXI, texture and color enhancement imaging.)

These data were measured using heterogeneous definitions across studies, such as diagnostic observation time alone in the study by Ezoe et al. [28] versus total procedure duration in the study by Li et al. [30]. This variability precluded meaningful quantitative synthesis or statistical comparison. Consequently, the procedural time data are presented for descriptive purposes only and should be interpreted with caution. Adverse events were reported in only one study. Ezoe et al. documented two biopsy-related bleeding cases (0.6%). No other studies reported adverse events.

3.5. Data Extraction and Quality Assessment

Data extraction was performed independently by two reviewers using a predefined data collection form. Extracted data included study characteristics, patient demographics, details of the index tests and reference standards, diagnostic accuracy outcomes, and available information on procedural time and adverse events.

The risk of bias and applicability of the included studies were independently assessed by two reviewers using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies 2) tool [12]. This instrument evaluates four domains: patient selection, index test, reference standard, and flow and timing. Signaling questions were used to determine the risk of bias (low, high, or unclear) and concerns regarding applicability.

4. Statistical Analysis

According to the type of target lesion, included studies and their corresponding data were stratified into separate groups. A network NMA was conducted independently for each group to comparatively assess the diagnostic performance of the different endoscopic modalities.

For each target condition, evidence network plots were generated using R software (version 4.5.2). In these plots, each node represents an individual endoscopic modality, and the thickness of the connecting lines corresponds to the number of direct comparative studies.

A Bayesian NMA based on an ANOVA model was performed within the R environment. This model accommodates both single-arm and multi-arm studies by assuming that missing comparisons occur at random, thereby enabling the inclusion of all available data. The model estimated absolute diagnostic measures, including sensitivity, specificity, and DORs, as well as relative measures such as relative sensitivity and relative specificity [8]. In addition, a composite superiority index integrating sensitivity and specificity was calculated to rank the diagnostic performance of the modalities [9]. Compared with traditional diagnostic test accuracy meta-analysis that only pooled pairwise comparisons, this NMA allows simultaneous synthesis of all available evidence and provides relative rankings. However, the model assumes exchangeability across studies and modalities, which may not fully hold in practice. The superiority index combines sensitivity and specificity into a single metric, providing a balanced summary of diagnostic performance, but it should not replace clinical judgment based on specific clinical scenarios.

The transitivity assumption underlying the NMA was carefully considered. Potential effect modifiers, including publication year, geographic region, endoscopist experience, biopsy protocols, and histopathological definitions, may influence diagnostic accuracy. Although we could not adjust for these factors due to limited study-level data, we assessed the consistency between direct and indirect evidence using node-splitting methods and evaluated incoherence.

Model convergence and the reliability of posterior estimates were evaluated using multiple diagnostic criteria. Three independent Markov chains were run, and convergence was considered satisfactory when the Gelman–Rubin potential scale reduction factor (R-hat) was below 1.05 for all key parameters [13]. A minimum effective sample size exceeding 400 was required to ensure precise posterior estimation [14]. The proportion of divergent transitions was also monitored. The R code used for the ANOVA model is provided in the Appendix (see Supplementary Data. The R code of the ANOVA model).

For the grouping of lesions, we classified high-grade intraepithelial neoplasia and gastric neoplasms together because most primary studies reported them as a combined outcome. This grouping may introduce heterogeneity, as the diagnostic criteria and endoscopic features differ between these lesions. We acknowledge this limitation and discuss its potential impact on the results.

Heterogeneity was quantified using random-effects parameters. Between-study variance was characterized by τ^2, reflecting variability in true diagnostic accuracy across studies, while the intra-class correlation coefficient (ICC) represented the degree of correlation among measurements of different modalities within the same study. A higher ICC indicates a greater influence of study-level characteristics [8].

5. Results

5.1. Study Characteristics

A total of 22 studies comprising 11,293 patients were included in the analysis [7,15-35]. The study selection process is illustrated in the PRISMA flow diagram (Figure 1).

Data for the diagnostic evaluation of gastric atrophy were obtained from four studies [15,26, 30,34], which collectively assessed four endoscopic modalities: WLE, NBI, CE, and CLE. For the diagnosis of intestinal metaplasia (IM), 13 studies were included, evaluating eight endoscopic modalities: WLE, NBI, BLI, LCI, AFE, CLE, OE, and CE [7,18,19,22,25-27,29-34]. Evidence for low-grade intraepithelial neoplasia (LGIN) was limited, with quantitative data available from only three studies [22,27,33], two of which reported results exclusively for CLE [27, 33]. Given the insufficient and imbalanced data, a network meta-analysis for LGIN was not feasible. The available data are presented in the Appendix (see Supplementary Table 2). Therefore, our findings for precancerous lesions mainly apply to atrophy and IM, and caution is needed when extrapolating to LGIN. For high-grade intraepithelial neoplasia and gastric neoplasms (HGIN/GN), most studies reported these outcomes as a combined category. Therefore, they were analysed as a single group. A total of 10 studies contributed data for HGIN/GN, assessing seven endoscopic modalities: WLE, NBI, BLI, LCI, CLE, TXI, and AFE [16,17,20-24,28, 33,35]. The evidence network plots are shown in Figure 2. Detailed characteristics of the included studies and patient populations are summarized in Table 1.

Table 1: Characteristics of included studies.

Study	Country	Study design	Mean age / Media age	Sample size	Sex (M/F)	Diagnosis	Index tests
Kato 2007(16)	Japanese	Prospective, single-center study	66.7	51	41/10	HGIN/GN	WLE/AFE
Capelle 2010(29)	Holland	Prospective, single-center study	58.7	43	28/15	IM	WLE/NBI
Ezoe 2011(28)	Japanese	Prospective, multicenter study	69	353	278/75	HGIN/GN	WLE/NBI
Li 2011(23)	China	Prospective, single-center study	58.1	1572	1038/534	HGIN/GN	WLE/CLE
Dutta 2013(30)	India	Prospective crossover study	52.3	200	132/68	Atrophy, IM	WLE/NBI
Fukuta 2013(25)	Japanese	Prospective, multicenter study	66	163	90/73	IM	WLE/CE
Lim 2013(18)	China	Prospective, single-center study	62.5	20	5/15	IM	WLE/AFE/ NBI/ CLE
So 2013(26)	Singapore	Prospective crossover study	61	64	29/35	Atrophy, IM	WLE/NBI
Xirouchakis 2013(34)	Greece	Prospective, single-center study	46	119	65/54	Atrophy, IM	WLE/NBI
Li 2014(27)	China	Prospective, single-center study	55	168	91/77	IM, LGIN	CLE
Gong 2015(35)	China	Prospective, single-center study	59.3	82	58/24	HGIN/GN	CLE/NBI
Liu 2015(15)	China	Prospective, single-center study	49.75	87	48/39	Atrophy	CE/NBI/CLE
Dohi 2017(20)	Japanese	Prospective, single-center study	70.2	118	95/23	HGIN/GN	WLE/BLI
Zuo 2017(33)	China	Prospective, multicenter study	55	120	74/46	IM, LGIN, HGIN/ GN	CLE
Chen 2019(32)	China	Prospective, single-center study	53.5	107	64/43	IM	WLE/LCI
Yang 2019(22)	China	Prospective, single-center study	56	235	144/91	IM, LGIN, HGIN/ GN	WLE/BLI
Ji 2020(31)	China	Prospective, single-center study	53.4	149	96/53	IM	OE/CE
Song 2021(19)	China	Prospective, single-center study	58.7	156	83/73	IM	WLE/OE/CE
Yoshida 2021(24)	Japanese	Prospective, multicenter study	70.6	4472	3527/945	HGIN/GN	WLE/NBI
Min 2022(21)	China	Prospective, multicenter study	57	1828	1038/790	HGIN/GN	WLE/LCI
Kadota 2024(17)	Japanese	Prospective, multicenter study	73	901	683/218	HGIN/GN	WLE/NBI/ TXI
Wan 2025(7)	China	Prospective, single-center study	57.16	285	175/110	IM	WLE/OE

(IM, intestinal metaplasia; LGIN, low-grade intraepithelial neoplasia; HGIN, high-grade intraepithelial neoplasia; GN, gastric neoplasms; WLE, white light endoscopy; NBI, narrow-band imaging; AFE, autofluorescence endoscopy; CLE, confocal laser endomicroscopy; CE, chromoendoscopy; BLI, blue laser imaging; LCI, linked color imaging; OE, optical enhancement; TXI, texture and color enhancement imaging).

Table 2: Summary of the comparative diagnostic efficacy of different modalities for atrophy, IM and HGIN/GN.

Endoscopy	Sensitivity	Specificity	Diagnostic odds ratio	Superiority index	Relative sensitivity	Relative specificity
Diagnostic efficacy for gastric atrophy						
WLE	0.52(0.35,0.67)	0.92(0.78,0.97)	15.93(3.61,42.39)	1.31(0.14,5.00)	0.85(0.41,2.15)	1.22(0.91,2.41)
NBI	0.68(0.62,0.74)	0.86(0.82,0.89)	13.42(8.52,20.28)	1.24(0.20,5.00)	1.11(0.69,2.68)	1.14(0.90,2.26)
CLE	0.77(0.32,0.98)	0.85(0.44,0.96)	101.44(1.59,600.34)	3.37(0.20,7.00)	1.24(0.48,2.87)	1.11(0.62,1.96)
CE	0.69(0.26,0.96)	0.79(0.38,0.94)	29.73(0.78,164.19)	1.25(0.14,5.00)	1.00	1.00
Diagnostic efficacy for IM						
WLE	0.54(0.47,0.61)	0.79(0.73,0.82)	4.47(2.81,6.42)	0.20(0.09,0.60)	0.88(0.59,1.61)	1.50(0.90,2.79)
NBI	0.77(0.65,0.86)	0.67(0.53,0.79)	7.64(2.94,16.38)	0.39(0.09,1.40)	1.25(0.83,2.28)	1.27(0.75,2.36)
BLI	0.68(0.37,0.89)	0.82(0.54,0.97)	23.33(1.51,112.57)	1.88(0.08,11.00)	1.10(0.54,2.07)	1.56(0.82,3.01)
LCI	0.88(0.65,0.98)	0.83(0.48,0.96)	127.61(4.69,635.48)	7.79(0.14,15.00)	1.43(0.87,2.64)	1.59(0.71,2.99)
CLE	0.91(0.79,0.97)	0.80(0.58,0.95)	77.80(9.69,313.11)	6.59(0.56,15.00)	1.48(1.01,2.68)	1.52(0.93,2.92)
OE	0.84(0.70,0.93)	0.86(0.70,0.95)	47.65(9.79,133.26)	5.39(0.43,13.00)	1.37(0.90,2.51)	1.64(0.95,3.05)
CE	0.81(0.67,0.91)	0.84(0.66,0.93)	32.82(6.83,92.53)	3.61(0.20,11.00)	1.32(0.87,2.40)	1.61(0.89,2.99)
AFE	0.66(0.34,0.89)	0.57(0.28,0.86)	4.62(0.41,20.58)	0.24(0.07,1.40)	1.00	1.00
Diagnostic efficacy for HGIN/GN						
WLE	0.68(0.61,0.74)	0.84(0.78,0.87)	11.33(6.98,16.68)	0.34(0.09,0.71)	1.17(0.79,2.00)	2.24(1.08,5.58)
NBI	0.79(0.67,0.88)	0.91(0.82,0.96)	48.07(14.44,106.13)	1.65(0.43,7.00)	1.36(0.90,2.35)	2.44(1.16,6.09)
BLI	0.92(0.81,0.98)	0.94(0.81,0.98)	347.05(41.16,1312.91)	8.55(1.67,13.00)	1.59(1.07,2.72)	2.50(1.19,6.27)
LCI	0.82(0.58,0.95)	0.79(0.46,0.95)	38.78(2.59,159.90)	1.48(0.11,9.00)	1.41(0.83,2.45)	2.12(0.83,5.36)
CLE	0.88(0.76,0.95)	0.97(0.91,0.99)	456.75(57.73,1567.99)	8.88(1.67,13.00)	1.51(1.01,2.58)	2.60(1.25,6.53)
TXI	0.81(0.52,0.98)	0.78(0.47,0.95)	47.80(2.27,243.48)	1.53(0.09,7.00)	1.40(0.76,2.47)	2.09(0.83,5.22)
AFE	0.61(0.34,0.84)	0.45(0.15,0.77)	2.09(0.19,8.96)	0.10(0.08,0.27)	1.00	1.00

(IM, intestinal metaplasia; LGIN, low-grade intraepithelial neoplasia; HGIN, high-grade intraepithelial neoplasia; GN, gastric neoplasms; WLE, white light endoscopy; NBI, narrow-band imaging; AFE, autofluorescence endoscopy; CLE, confocal laser endomicroscopy; CE, chromoendoscopy; BLI, blue laser imaging; LCI, linked color imaging; OE, optical enhancement; TXI, texture and color enhancement imaging.).

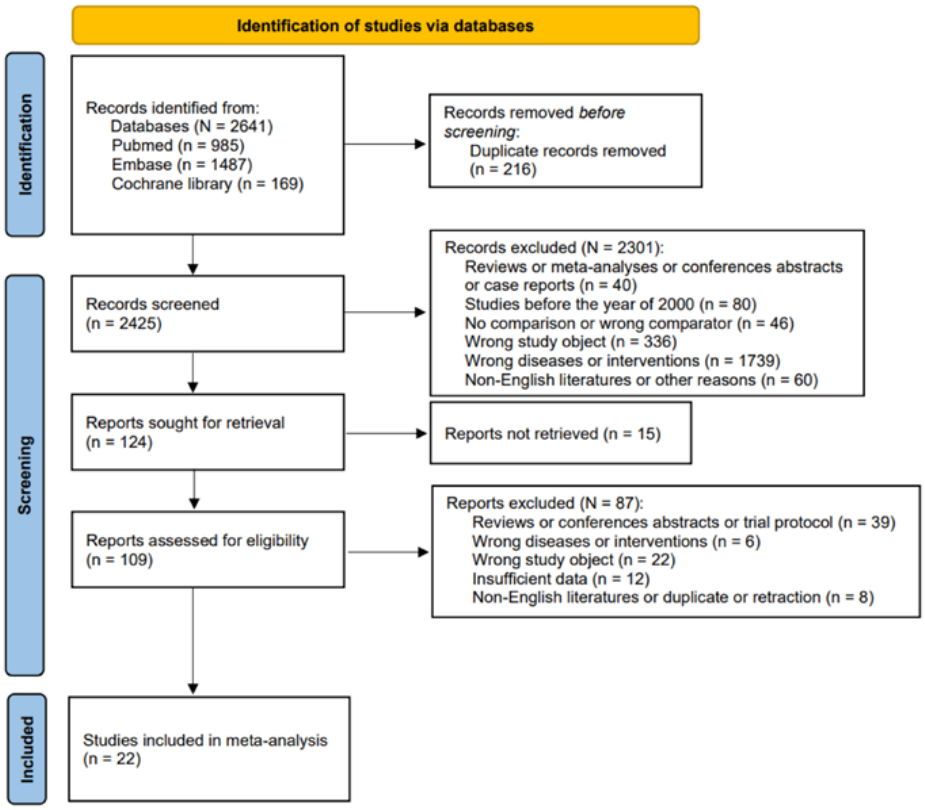

Figure 1: Flow chart of literature search.

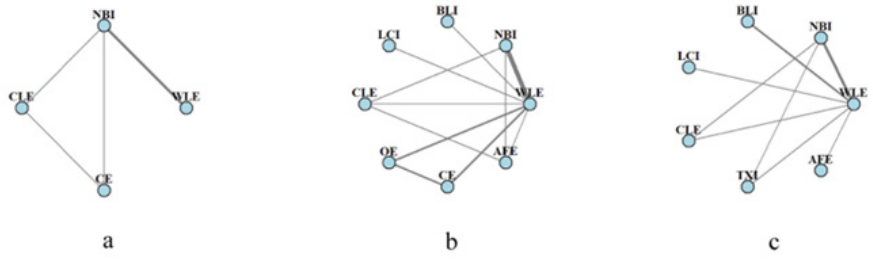

Figure 2: Network plots of the index tests: (a) diagnosis of atrophy; (b) diagnosis of intestinal metaplasia; (c) diagnosis of high-grade intraepithelial neoplasia and gastric neoplasms. WLE: white light endoscopy; NBI: narrow-band imaging; AFE: autofluorescence endoscopy; CLE: confocal laser endomicroscopy; CE: chromoendoscopy; BLI: blue laser imaging; LCI: linked colour imaging; OE: optical enhancement; TXI: texture and colour enhancement imaging.

5.2. Study Quality and Heterogeneity

The methodological quality of the 22 included studies was assessed using the QUADAS-2 tool [12], and the summary of the assessment is presented in Figure 3. One study by Kato et al. was judged to have a high risk of selection bias due to its case–control design. Studies by Capelle et al., Lim et al., Xirouchakis et al., and Yang et al. did not clearly report whether patient enrolment was consecutive or random, which may introduce potential selection bias.

Across the remaining QUADAS-2 domains-index test, reference standard, and flow and timing the included studies generally demonstrated a low risk of bias. Detailed estimates of τ^2 (between-study variance) and the ICC are provided in the Appendix (see Supplementary Table 3). In general, the τ^2 values were modest, indicating moderate heterogeneity. Notably, the use of magnification versus non-magnification endoscopy and difference in histopathological criteria were not accounted for, which may contribute to unexplained heterogeneity.

Local inconsistency was assessed using the node-splitting method. For the key comparisons with both direct and indirect evidence, the Bayesian p-values were all above 0.05. These results indicate no statistically significant local inconsistency in the network, supporting the consistency assumption of the network meta-analysis estimates. Detailed inconsistency results are presented in Supplementary Table 4.

5.3. Diagnostic Efficacy for Atrophy

For the diagnosis of gastric atrophy, the results indicated that CLE demonstrated the highest sensitivity (0.77, 95% CI: 0.32–0.98), whereas WLE exhibited the highest specificity (0.92, 95% CI: 0.78–0.97). According to the superiority index, CLE was ranked first, followed by WLE, CE, and NBI (Figure 4a and Table 2).

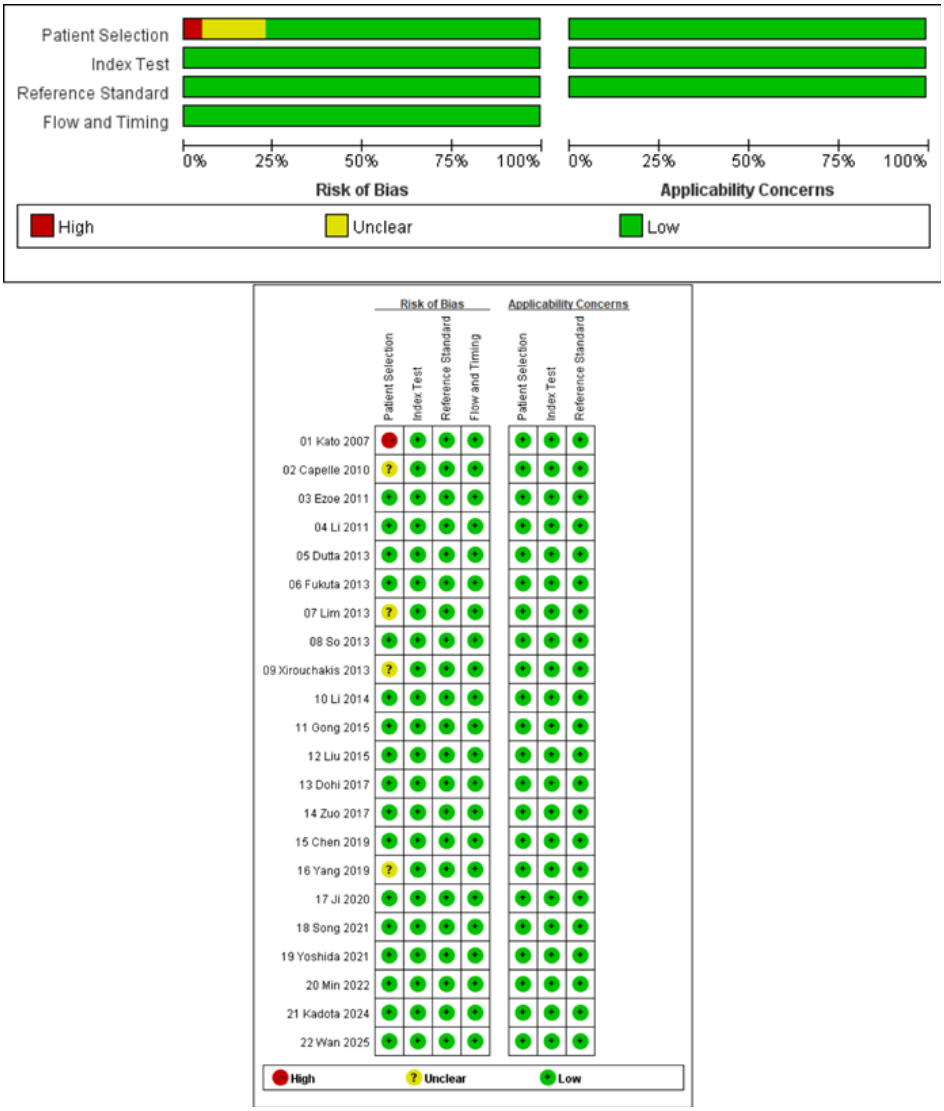

Figure 3: Quality assessment of the studies included using the modified Quality Assessment of Diagnostic Accuracy Studies 2.

5.4. Diagnostic Efficacy for IM

With respect to the detection of IM across the eight evaluated endoscopic modalities, the network meta-analysis revealed a clear hierarchy of diagnostic performance. CLE again demonstrated the highest sensitivity (0.91, 95% CI: 0.79–0.97); however, its specificity (0.80, 95% CI: 0.58–0.95) was lower than that of OE (0.86, 95% CI: 0.70–0.95), CE (0.84, 95% CI: 0.66–0.93), LCI (0.83, 95% CI: 0.48–0.96), and BLI (0.82, 95% CI: 0.54–0.97). WLE and AFE were associated with the poorest sensitivity and specificity, respectively. Based on the superiority index, the overall ranking in descending order was as follows: LCI, CLE, OE, CE, BLI, NBI, AFE, and WLE (Figure 4b and Table 2).

5.5. Diagnostic Efficacy for HGIN/GN

Direct and indirect comparisons among the endoscopic modalities were synthesized using Bayesian NMA. As shown in Figure 4c and Table 2, CLE ranked first in terms of specificity (0.97, 95% CI: 0.91–0.99), whereas its sensitivity (0.88, 95% CI: 0.76–0.95) was second only to that of BLI (0.92, 95% CI: 0.81–0.98). In contrast, AFE yielded the lowest estimates for both sensitivity (0.61, 95% CI: 0.34–0.84) and specificity (0.45, 95% CI: 0.15–0.77). According to the superiority index, CLE was identified as the most strongly recommended modality, followed by BLI, NBI, TXI, LCI, WLE, and AFE.

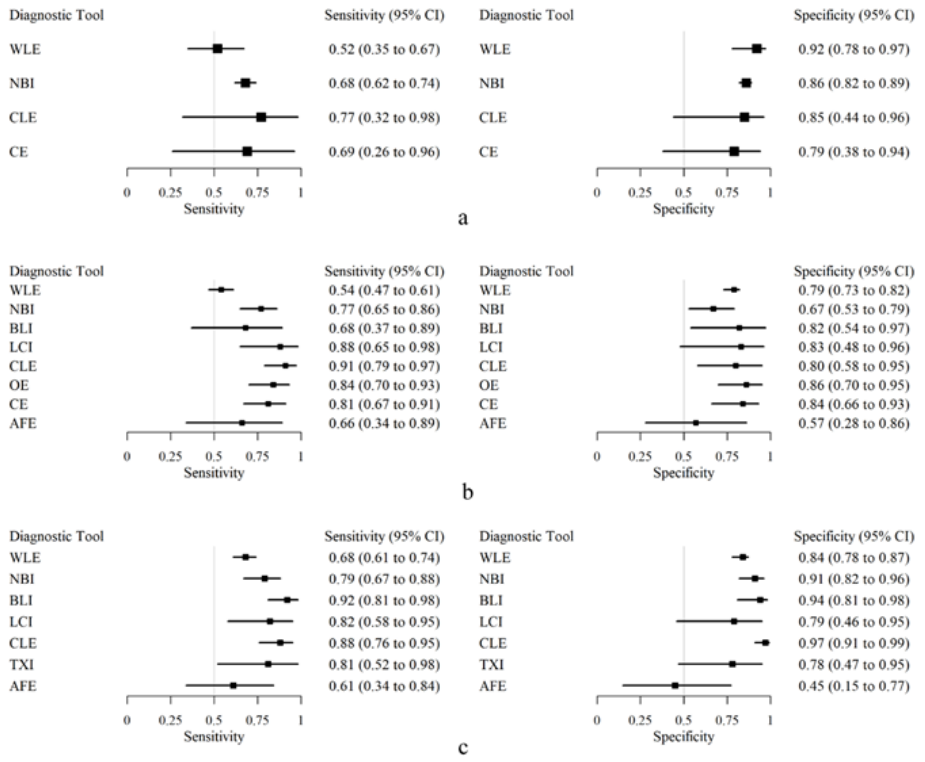

Figure 4: Forest plots of pooled sensitivity and specificity of the index techniques for (a) diagnosis of atrophy; (b) diagnosis of IM; (c) diagnosis of HGIN/GN. IM: intestinal metaplasia; HGIN: high-grade intraepithelial neoplasia; GN: gastric neoplasms; WLE: white light endoscopy; NBI: narrow-band imaging; AFE: autofluorescence endoscopy; CLE: confocal laser endomicroscopy; CE: chromoendoscopy; BLI: blue laser imaging; LCI: linked colour imaging; OE: optical enhancement; TXI: texture and colour enhancement imaging.

6. Discussion

Gastric cancer continues to represent a major global health challenge, with prognosis critically dependent on early detection. Although the diagnostic armamentarium has expanded beyond WLE to include a range of image-enhanced and virtual histology techniques, comparative evidence regarding their diagnostic efficacy across the full spectrum of gastric precancerous lesions has remained fragmented. Previous meta-analyses have assessed the diagnostic performance of individual endoscopic modalities. For example, one meta-analysis reported that magnifying endoscopy with narrow-band imaging (M-NBI) and magnifying endoscopy with blue laser imaging (M-BLI) outperformed WLE in the detection of early gastric cancer [36]. In addition, several meta-analyses have demonstrated the excellent diagnostic performance of CLE for various gastric pathologies [37-39]. However, these studies typically focused on a single modality or a specific lesion type and lacked comprehensive comparisons across different categories of endoscopic technologies and the entire pathological continuum. By applying a Bayesian NMA based on an ANOVA model, the present study synthesized both direct and indirect evidence across a broad range of endoscopic modalities and lesion types.

The principal finding of this analysis is the identification of a clear performance gradient among endoscopic technologies. CLE emerged as the highest-ranked modality for the diagnosis of atrophy, intestinal metaplasia, and high-grade intraepithelial neoplasia or gastric neoplasms, ranking first for atrophy and HGIN/GN and second for IM. The superior diagnostic performance of CLE is primarily attributable to its ability to provide in vivo histological assessment. This technique enables real-time, cellular-level imaging, allowing direct visualization of key pathological features such as nuclear enlargement, hyperchromasia, and glandular architectural distortion [40, 41]. By narrowing the gap between endoscopic assessment and histopathological diagnosis, CLE offers a substantial advantage for targeted biopsy and immediate diagnostic confidence, particularly in high-risk clinical settings.

Following CLE, advanced image-enhanced endoscopy techniques, particularly BLI and LCI, demonstrated superior diagnostic performance compared with WLE. The high performance of BLI can be attributed to its laser-based, high-intensity illumination, which markedly enhances microvascular and mucosal surface contrast and facilitates the detection of subtle neoplastic changes [42]. The strong performance of LCI, especially for IM, is likely related to its post-processing algorithms that accentuate colour differences, thereby improving the recognition of subtle mucosal features such as light blue crests. In contrast, the relatively lower performance of WLE highlights the intrinsic limitations of conventional imaging in detecting subtle gastric lesions.

The lesion-specific analyses revealed important nuances. For IM, a key and potentially reversible precancerous stage, both virtual histology (CLE) and high-contrast image-enhanced or dye-based techniques (LCI, OE, and CE) demonstrated high diagnostic efficacy. This finding suggests that accurate diagnosis of IM relies heavily on the recognition of characteristic colour and surface patterns, which are enhanced by these modalities. In contrast, the

evidence base for the diagnosis of atrophic gastritis was relatively limited, underscoring a gap in high-quality comparative research in this area.

The clinical implications of this diagnostic hierarchy are substantial, but they must be weighed against practical considerations. CLE, despite its high performance, requires expensive equipment and extensive training, limiting its availability to tertiary centres. Its workflow burden makes it less suitable for routine screening. In contrast, image-enhanced techniques such as BLI, LCI, and NBI are more readily integrated into standard endoscopy systems, with shorter learning curves and lower incremental costs, making them practical for large-scale screening and surveillance programs. Therefore, the choice of modality should balance diagnostic efficacy against resource availability and clinical setting, distinguishing between high-accuracy diagnosis in selected patients versus efficient screening in average-risk populations.

It is crucial to emphasize that histopathological examination remains the gold standard for diagnosis of gastric lesions. Endoscopic modalities, regardless of their accuracy, serve as screening and triage tools, and all suspicious findings should be confirmed by biopsy or resection.

However, several limitations should be acknowledged. The evidence base was asymmetric. Data available for the LGIN subgroup were limited, precluding a meaningful NMA; consequently, no pooled estimates could be generated for this condition. Moreover, although evidence for IM and HGIN/GN was relatively abundant, the small number of studies addressing atrophic gastritis may reduce the robustness of the corresponding findings. In addition, several potentially promising modalities, such as AFE and TXI, were evaluated in single studies only, resulting in increased uncertainty of the effect estimates.

The ranking results, particularly the superiority index, should be interpreted with caution. For modalities with limited evidence, the estimated ranks have wide uncertainty. The wide confidence intervals for some estimates reflect sparse data, and the observed hierarchy may not be stable. Therefore, these rankings should be considered exploratory rather than definitive, and clinical decisions should rely on the totality of evidence, not solely on rank. Furthermore, the present analysis focused exclusively on diagnostic accuracy metrics. Key factors influencing clinical adoption, including cost-effectiveness, learning curves, and equipment availability, were not assessed, despite their importance for real-world implementation.

The evidence gaps identified in this study indicate directions for future research. Specifically, high-quality studies focusing on the endoscopic diagnosis of LGIN and atrophic gastritis are needed. In addition, exploration of the integration of artificial intelligence with advanced endoscopic imaging represents a promising avenue for standardizing interpretation and improving diagnostic accuracy. Combining multiple imaging modalities or integrating artificial intelligence with advanced endoscopy may improve diagnostic consistency and reduce interobserver variability. Future research should explore these synergistic approaches. Furthermore, structured image interpretation protocols and risk stratification models can be integrated with endoscopic findings to guide clinical decision-making. For example, combining endoscopic grading with patient risk factors may optimize surveillance intervals and biopsy strategies. The development of decision-support systems that incorporate both endoscopic ad clinical data represents a promising direction for personalized management.

In summary, this network meta-analysis consolidates fragmented comparative evidence and establishes a diagnostic hierarchy among contemporary endoscopic modalities for gastric neoplasms and major precancerous lesions. CLE demonstrated high diagnostic performance, particularly for atrophy and neoplasia, owing to its capability for in vivo histological assessment. Advanced image-enhanced endoscopy techniques also showed superior diagnostic efficacy compared with standard WLE. Nonetheless, all findings should be interpreted in the context of evidence strength and clinical feasibility.

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