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ORIGINAL ARTICLE – HEALTHCARE POLICY AND OUTCOMES

How Good is Endoscopic Ultrasound in Differentiating Various T Stages of Rectal Cancer? Meta-Analysis and Systematic Review

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ABSTRACT Published data on accuracy of endoscopic ultrasound (EUS) in differentiating T stages of rectal cancers is varied. Study selection criteria were to select only EUS studies confirmed with results of surgical pathology. Articles were searched in Medline and Pubmed. Pooling was conducted by both fixed and random effects models. Initial search identified 3,630 reference articles, of which 42 studies ($N = 5{,}039$) met the inclusion criteria and were included in this analysis. The pooled sensitivity and specificity of EUS to determine T1 stage was 87.8% [95% confidence interval (CI) 85.3–90.0%] and 98.3% (95% CI 97.8–98.7%), respectively. For T2 stage, EUS had a pooled sensitivity and specificity of 80.5% (95% CI 77.9–82.9%) and 95.6% (95% CI 94.9–96.3%), respectively. To stage T3 stage, EUS had a pooled sensitivity and specificity of 96.4% (95% CI 95.4–97.2%) and 90.6% (95% CI 89.5–91.7%), respectively. In determining the T4 stage, EUS had a pooled sensitivity of 95.4% (95% CI 92.4–97.5%) and specificity of 98.3% (95% CI 97.8–98.7%). The p value for chi-squared heterogeneity for all the pooled accuracy estimates was > 0.10. We conclude that, as a result of the demonstrated sensitivity and specificity, EUS should be the investigation of choice to T stage rectal cancers. The sensitivity of EUS is higher for advanced disease than for early disease. EUS should be strongly considered for T staging of rectal cancers.

Rectal cancer affects many patients worldwide, specifically Western Europe and North America. In 2004, invasive rectal cancer was found in 13.1 patients per 100,000 in the USA with rectal cancer being diagnosed in approximately 41,000 patients in the USA yearly.[1,2] Although most rectal cancers are localized, approximately 15% have distant metastasis, with approximately 6% not staged for various reasons.[2] Many risk factors for rectal cancers exist, including familial polyposis syndromes obesity, diabetes mellitus, history of adenomatous polyps, excessive alcohol, and cigarette smoking.[3–7] As the risk factors of alcohol use and smoking remain prominent, with obesity increasing in the USA, timely diagnosis and adequate treatment for rectal cancer are crucial. However, before treatment, it is imperative to evaluate extent of the disease with staging.

In rectal cancers, the tumor–node–metastasis (TNM) staging guides treatment decisions and prognosis.[8] The TNM staging for rectal cancer is bases upon the depth of invasion of the lesion (T), the extent of regional lymph node invasion (N), and the presence of distant metastasis (M). Tis lesions are defined as those tumors confined to the epithelial or the lamina propria. T1 lesions are slightly more advanced and there is evidence of invasion into the submucosa. If the malignancy has involved the muscularis without transmural invasion, the tumor is staged T2. T3 lesions have invasion into the subserosa or into the non-peritonized pericolic or perirectal tissues. T4 lesions, the most advanced T stage, exhibit extension into other structures and/or perforate the visceral peritoneum.

Stage 0 disease, associated with the best prognosis, represents Tis without any lymph node involvement (N0) or distant metastasis (M0). Stage I disease (T1N0M0 and T2M0N0 lesions) correlates to a 5-year survival rate of approximately 85–90%.[2,9–11] Stage II disease (T3N0M0 and T4N0M0 lesions) exhibits a 5-year survival rate of approximately 60–65%.[2,9–11] Stage III disease (T1-4N1-2M0) represents any T level with one or two lymph nodes invaded but no distant metastasis, and correlates with a 5-

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year survival rate of approximately 30–40%.[9–11] Stage IV disease, the most severe, represents evidence of distal metastasis (T1-4N1-2M1) with the 5-year survival rate estimated to be approximately 8–9%.[2] As the disease becomes advanced, marked decrease in survival is observed.

Optimal management of rectal cancer varies with the stage of disease, and may involve the use of surgery, chemotherapy, and/or radiation therapy. The difference in the available treatment regimens emphasizes the importance of accurate staging. Stage 0 tumors may be managed with local excision of the lesion and/or radiation therapy.[12–14] Stage I lesions may be treated with surgical excision alone, either low abdominal resection or abdominal perineal resection depending on the location of the lesion, radiation therapy alone, or combination of surgery and radiation.[12,13,15,16] Stage II and III rectal cancers have a high local recurrence rate after surgery alone.[2,16] Stage II and III lesions have a significantly reduced recurrence and distant metastasis with improved survival with combined approach of surgical removal, chemotherapy, and radiation therapy as compared with surgery and radiation alone.[2,17] In patients with stage IV disease, improved rates of resectability with possibly local control and survival can be achieved by combining moderate- to high-dose preoperative radiation therapy with concurrent 5-fluourouracil (5-FU)-based chemotherapy.[2,18] Therefore, appropriate staging significantly guides treatment.

To determine the TNM stage, many modalities have been utilized, from computed tomography (CT) of the abdomen, magnetic resonance imaging (MRI) of the abdomen, to endoscopic ultrasound (EUS). The T stage accuracy of CT abdomen is 65–75% and that of MRI is 75–85%, but all with varying results.[19–25]. CT of the abdomen has been associated with underestimation of the T stage as compared with transrectal EUS.[26] Also, CT and MRI lack the ability to differentiate layers of the bowel wall.

With such major differences in the approach for T2 (stage I) and T3 (stage II) disease, the accuracy of T staging is pivotal in aiding the clinician in deciding on a course of therapy. The accuracy of T staging of rectal cancers by EUS has varied considerably in the literature. Due to this inconsistency and the importance of accurate staging for treatment and prognosis, we performed a meta-analysis to evaluate the accuracy of EUS in T staging of rectal cancers.

This meta-analysis and systematic review was written in accordance with the proposal for reporting by the quality of reporting of meta-analyses (QUOROM) statement.[27] Since this manuscript looks at diagnostic accuracy of a test, the study design for this meta-analysis and systematic review followed the guidelines of the Standards for Reporting of Diagnostic Accuracy (STARD) initiative.[28]

METHODS

Study Selection Criteria

Only EUS studies based upon the standard of surgical histology were selected. The EUS criteria used for determining the T stage were: T1, a focal hypoechoic mass in contact with the lamina propria or submucosa but without evidence of invasion into the muscularis propria; T2, a focal hypoechoic mass invading into the muscularis propria; T3, the focal hypoechoic mass invades through the muscularis propria and comes into contact with adjacent structures; and T4, the hypoechoic mass invades adjacent structures. From this pool, only studies from which a 2×2 table could be constructed for true positive, false negative, false positive, and true negative values were included.

Data Collection and Extraction

Articles were searched in MEDLINE (through PubMed, an electronic search engine for published articles and Ovid), Pubmed, Ovid journals, Cumulative Index for Nursing & Allied Health Literature, American College of Physicians (ACP) journal club, Database of abstracts of Reviews of effectiveness (DARE), International Pharmaceutical Abstracts, old Medline, Medline nonindexed citations, OVID Healthstar, and Cochrane Central Register of Controlled Trials (CENTRAL). The search was performed for the years 1980 to January 2008. The terms used for search were endoscopic ultrasound, EUS, ultrasound, endosonography, rectal cancer, tumor staging, staging, surgery, sensitivity, specificity, positive predictive value, and negative predictive value. Study authors were

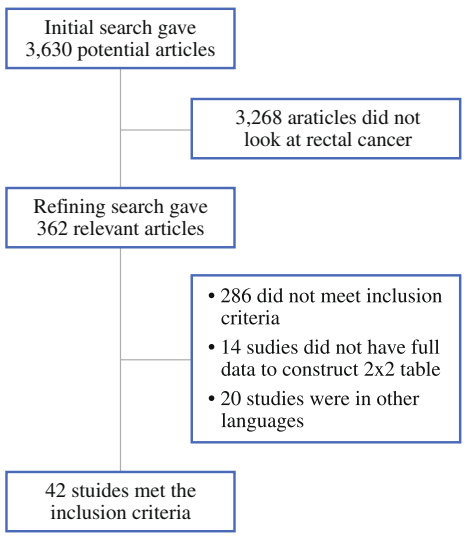

FIG. 1 Search results

TABLE 1 Characteristics of studies included in this analysis

	Author and year	Cancer	Type of study	Confirmatory procedure
1	Saitoh et al., 1986	Rectal cancers	Consecutive	Surgery
2	Waizer et al., 1989	Rectal cancers	Prospective	Surgery
3	Bali et al., 2004	Rectal cancers	Consecutive	Surgery
4	Zbar et al., 2004	Rectal cancers	Consecutive	Surgery
5	Sailer et al., 1997	Rectal cancers	Prospective	Surgery
6	Glaser et al., 1992	Rectal cancers	Consecutive	Surgery
7	Maor et al., 2006	Rectal cancers	Consecutive	Surgery
8	Kim et al., 2006	Rectal cancers	Consecutive	Surgery
9	Akasu et al., 2000	Rectal cancers	Consecutive	Surgery
10	Norotn et al., 1999	Rectal cancers	Consecutive	Surgery
11	Kaneko et al., 1995	Rectal cancers	Consecutive	Surgery
12	Adams et al., 1998	Rectal cancers	Consecutive	Surgery
13	Gualdi et al., 2000	Rectal cancers	Consecutive	Surgery
14	Hildebrandt et al., 1984	Rectal cancers	Consecutive	Surgery
15	Mackay et al., 2003	Rectal cancers	Consecutive	Surgery
16	Nishimori et al., 1998	Rectal cancers	Consecutive	Surgery
17	Marone et al., 2000	Rectal cancers	Consecutive	Surgery
18	Hsieh et al., 2003	Rectal cancers	Consecutive	Surgery
19	Hildebrandt et al., 1986	Rectal cancers	Consecutive	Surgery
20	Massari et al., 1998	Rectal cancers	Consecutive	Surgery
21	Boyce et al., 1991	Rectal cancers	Consecutive	Surgery
22	Pappalardo et al., 1990	Rectal cancers	Consecutive	Surgery
23	Akasu et al., 2000	Rectal cancers	Consecutive	Surgery
24	Feifel et al., 1987	Rectal cancers	Consecutive	Surgery
25	Giovannini et al., 2006	Rectal cancers	Consecutive	Surgery
26	Marusch et al., 2002	Rectal cancers	Prospective	Surgery
27	Meyenberger et al., 2005	Rectal cancers	Consecutive	Surgery
28	Thaler et al., 1994	Rectal cancers	Consecutive	Surgery
29	Waizer et al., 1991	Rectal cancers	Consecutive	Surgery
30	Herzong et al., 1993	Rectal cancers	Prospective	Surgery
31	Nielsen et al., 1996	Rectal cancers	Consecutive	Surgery
32	Sentovich et al., 1993	Rectal cancers	Consecutive	Surgery
33	Romano et al., 1985	Rectal cancers	Consecutive	Surgery
34	Bianchi et al., 2006	Rectal cancers	Consecutive	Surgery
35	Ramana et al., 1997	Rectal cancers	Consecutive	Surgery
36	Garcia-Aguilar et al., 2002	Rectal cancer	Consecutive	Surgery
37	Manger et al., 2004	Rectal cancer	Consecutive	Surgery
38	Starck et al., 2003	Rectal cancer	Consecutive	Surgery
39	Kim et al., 2001	Rectal cancer	Consecutive	Surgery
40	Osti et al., 1997	Rectal cancer	Consecutive	Surgery
41	Caseiro-Alves et al., 1998	Rectal cancer	Consecutive	Surgery
42	Norton et al., 1999	Rectal cancer	Consecutive	Surgery

contacted when the required data could not be determined from the publications. Two-by-two tables were constructed with the data extracted from each study. Two authors (S.R.P. and J.B.K.R.) independently searched and extracted the data into an abstraction form. Any differences were resolved by mutual agreement. Agreement between reviewers for the collected data was quantified using Cohen's κ.[29]

Quality of Studies

Clinical trials designed with control and treatment arms can be assessed for quality of the study. A number of criteria have been used to assess this quality of a study (e.g., randomization, selection bias of the arms in the study, concealment of allocation, and blinding of outcome).[30,31] There is no consensus on how to assess studies designed without a control arm. Hence, these criteria do not apply to studies without a control arm.[31] Therefore, for this meta-analysis and systematic review, studies were selected based on completeness of data and inclusion criteria. Completeness was defined as data available for true positive, false negative, false positive, and true negative values of the diagnostic test (EUS). These determinations of accuracy of EUS staging were expressed using true positive (tumor stage confirmed), true negative (lack of a tumor stage confirmed), falsely positive (tumor overstaged), and falsely negative (tumor understaged). A nonvalidated criteria, the Quality Assessment of Studies of Diagnostic Accuracy Included in Systematic Reviews (QUADAS) criteria, has been proposed to evaluate quality of diagnostic studies.[32,33] This was also used to evaluate the studies on the 14 items described in the QUADAS criteria.

Statistical Methods

Meta-analysis for the accuracy of EUS in diagnosing T stage of rectal cancers was performed by calculating pooled estimates of sensitivity, specificity, likelihood ratios, and diagnostic odds ratios. EUS studies were grouped into periods of time to standardize the changes in EUS technology, experience of endoscopists, and EUS criteria for T involvement.[34–36] These periods of time were 1986–1994, 1995–2000, and 2001–2008. Pooling was conducted using both Mantel–Haenszel method

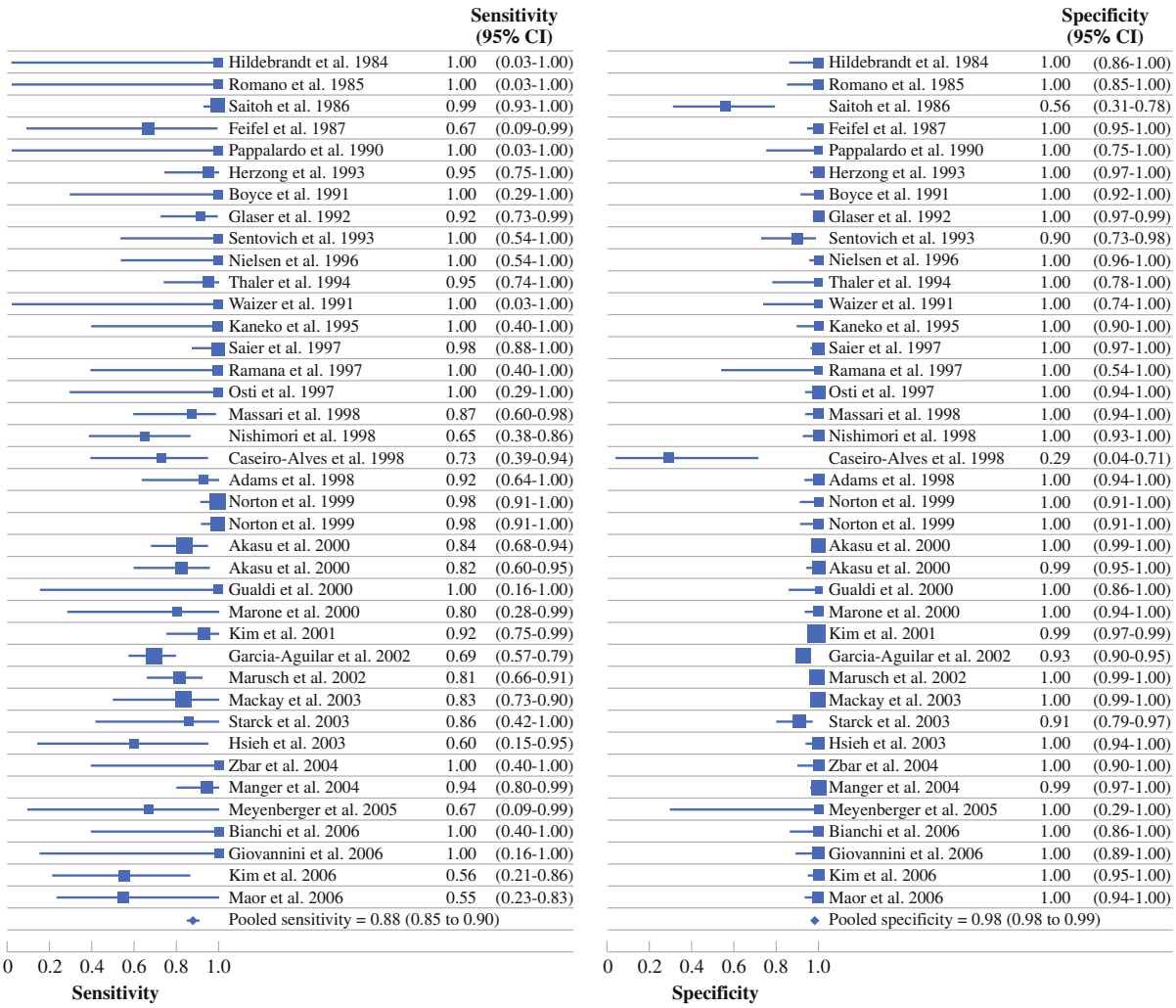

FIG. 2 Forrest plot showing sensitivity and specificity of EUS to diagnose T1 stage of rectal cancer

(fixed-effects model) and DerSimonian–Laird method (random-effects model). The confidence intervals were calculated using the *F* distribution method.[37] Forrest plots were drawn to show the point estimates in each study in relation to the summary pooled estimate. The width of the point estimates in the Forrest plots indicates the assigned weight to that study. For cells with zero value, a 0.5 was added as described by Cox.[38] The heterogeneity of the sensitivities and specificities were tested by applying the likelihood ratio test.[39] The heterogeneity of likelihood ratios and diagnostic odds ratios were tested using Cochran's *Q* test based upon inverse variance weights.[40] Heterogeneity among studies was also tested by using summary receiver operating characteristic (SROC) curves. SROC curves were used to calculate the area under the curve (AUC). The effect of publication and selection bias on the summary estimates was tested by Egger bias indicator and Begg–Mazumdar bias indicator.[41,42] Also, funnel plots were constructed to evaluate potential publication bias using the standard error and diagnostic odds ratio.[43,44]

RESULTS

Initial search identified 3,630 reference articles. Among these, 392 relevant articles were selected and reviewed. Data was extracted from 42 studies ($N = 5{,}039$) that met the inclusion criteria.[45–86] Figure 1 shows the search results. The characteristics of studies are shown in Table 1. The included 42 studies were published as full-text articles in peer review journals. All the pooled estimates given are estimates calculated by the fixed-effects model. The agreement analysis between the reviewers for data collected separately gave a kappa value of 1.0. QUADAS criteria to evaluate the quality of studies showed that all the studies fulfilled 4–5 out of 14 described criteria.

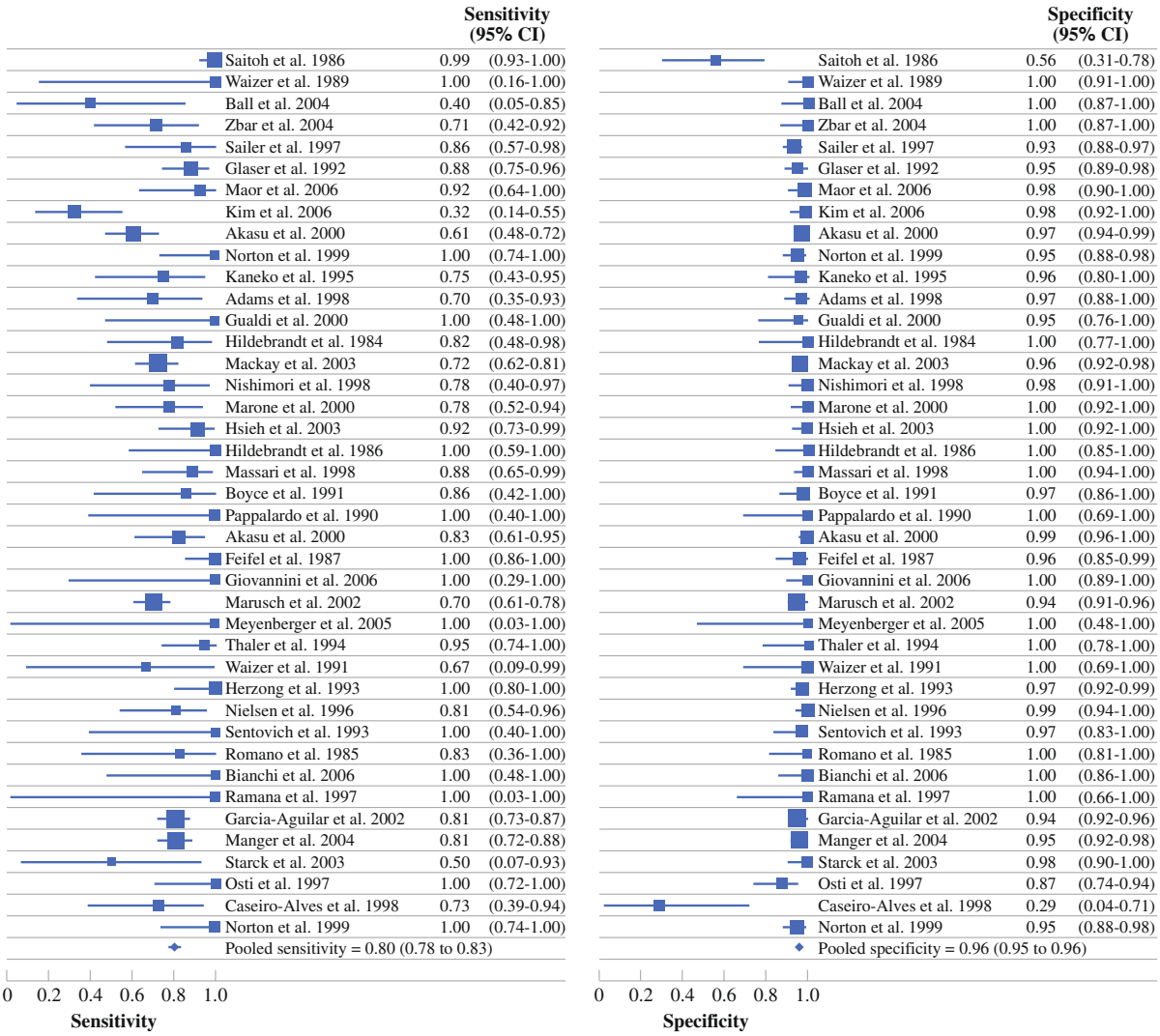

FIG. 3 Forrest plot showing sensitivity and specificity of EUS to diagnose T2 stage of rectal cancer

Accuracy of EUS to T-Stage Rectal Cancers

The pooled sensitivity and specificity of EUS to diagnose T1 stage cancer was 87.8% (95% CI 85.3–90.0%) and 98.3% (95% CI 97.8–98.7%), respectively. Figure 2 shows the sensitivity and specificity to determine T1 stage cancer in a Forrest plot. For T2 stage, EUS had a pooled sensitivity and specificity of 80.5% (95% CI 77.9–82.9%) and 95.6% (95% CI 94.9–96.3%), respectively. The Forrest plot in Fig. 3 shows the sensitivity and specificity of EUS to determine T2 stage cancer. For T3 stage, EUS had a pooled sensitivity and specificity of 96.4% (95% CI 95.4–97.2%) and 90.6% (95% CI 89.5–91.7%), respectively. Figure 4 shows the ability of EUS to determine stage T3 as a Forrest plot. To diagnose T4 stage cancer, EUS had a pooled sensitivity of 95.4% (95% CI 92.4–97.5%) and specificity of 98.3% (95% CI 97.8–98.7%). The sensitivity and specificity of EUS to determine T4 stage cancer from individual studies are shown as a Forrest plot in Fig. 5. A test of heterogeneity for all the pooled estimates for T stages had a p value > 0.10. All the pooled estimates calculated by fixed- and random-effect models were similar. Table 2 shows the pooled accuracy estimates of EUS to T-stage rectal cancers.

Effect of Technology over Time

EUS studies were grouped into three periods of time to standardize criteria for EUS imaging of lymph node involvement, improvement in endoscopists' experience, and changes in technology over the past two decades. These periods of time were 1984–1994, 1995–2000, and 2001–2008. The periods of time were chosen arbitrarily in association with major changes in the EUS technology and diagnostic criteria would have taken place during these periods of time. During these periods of time, the number

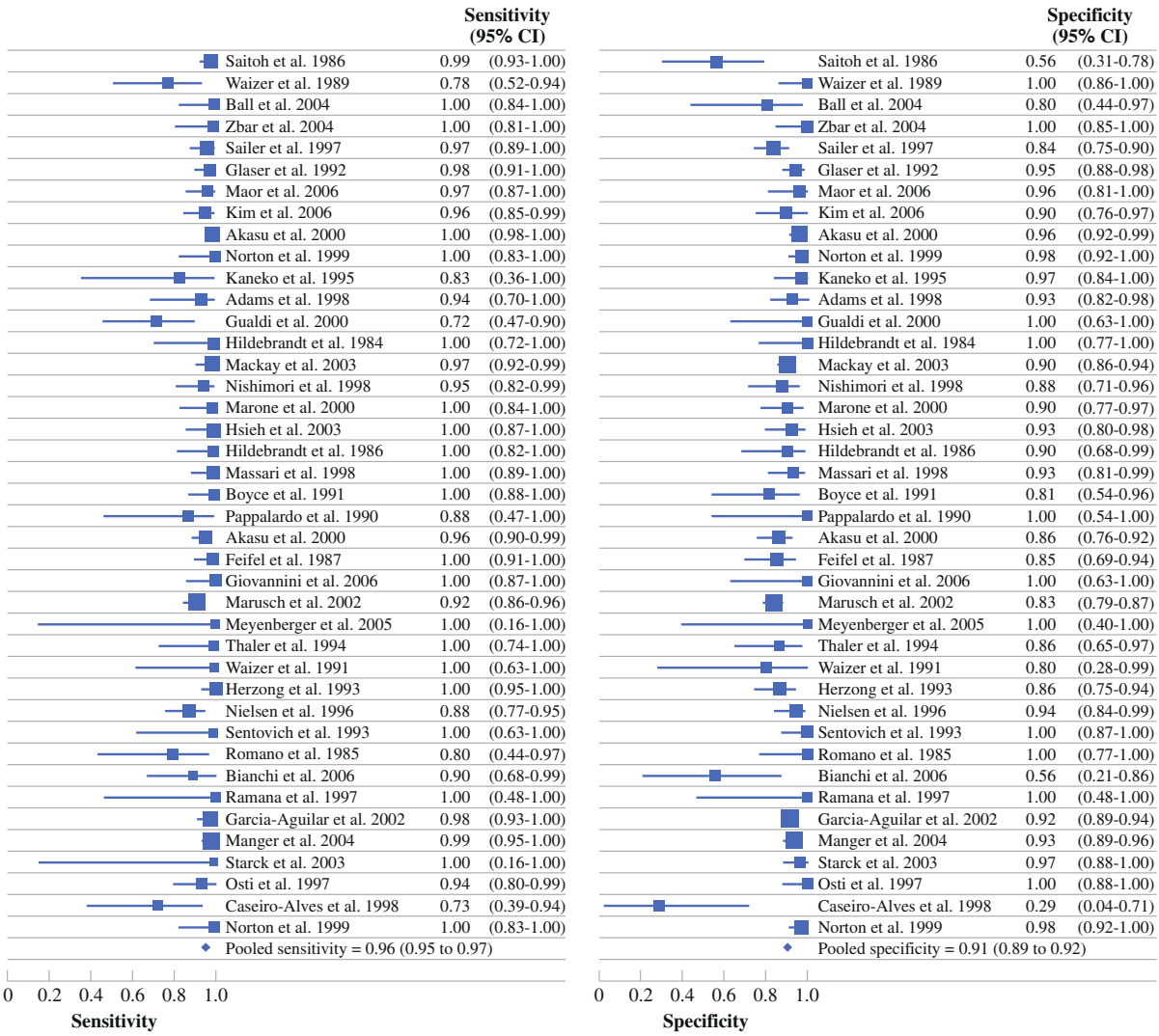

FIG. 4 Forrest plot showing sensitivity and specificity of EUS to diagnose T3 stage of rectal cancer

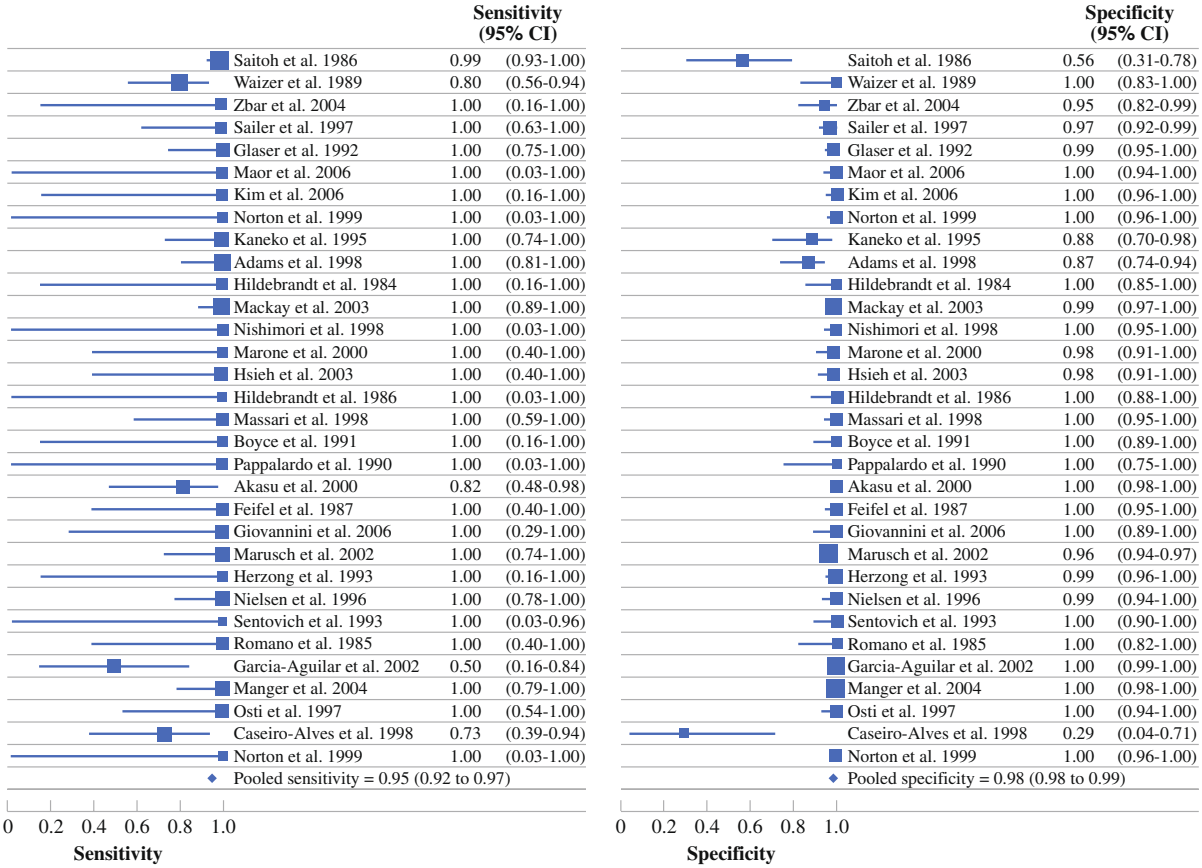

FIG. 5 Forrest plot showing sensitivity and specificity of EUS to diagnose T4 stage of rectal cancer

TABLE 2 Accuracy of EUS with confidence intervals to stage rectal cancer patients

	Pooled sensitivity	Pooled specificity	Pooled LR+	Pooled LR–	Pooled DOR
T1	87.8% (85.3–90.0%)	98.3% (97.8–98.7%)	44.0 (22.7–85.5)	0.16 (0.13–0.23)	333.9 (161.4–690.4)
T2	80.5% (77.9–82.9%)	95.6% (94.9–96.3%)	17.3 (11.9–24.9)	0.22 (0.17–0.29)	92.1 (64.2–132.2)
T3	96.4% (95.4–97.2%)	90.6% (89.5–91.7%)	8.9 (6.8–11.8)	0.06 (0.04–0.09)	204.9 (124.9–336.6)
T4	95.4% (92.4 –97.5%)	98.3% (97.8–98.7%)	37.6 (19.9–71.0)	0.14 (0.09–0.23)	367.6 (170.9–790.6)

LR+, positive likelihood ratio; LR–, negative likelihood ratio; *DOR*, diagnostic odds ratio

of studies that met the inclusion criteria for EUS as an imaging modality was 13, 11, and 10, respectively. All pooled estimates during the three periods of time are given in Table 3. The p value for chi-squared heterogeneity for all the pooled accuracy estimates was > 0.10.

Bias Estimates

The publication bias calculated by the Begg–Mazumdar and Harbord–Egger bias indicators for each stage of rectal cancer invasion is shown in Table 4. The bias indicators did not show any bias. The funnel plots in Fig. 6 shows no publication bias for EUS studies estimating T stages of rectal cancers.

SROC curves were drawn for AUC and Q values. The AUC and Q values of EUS to diagnose various stages of rectal cancer are shown in Table 4. SROC curves for T staging are shown in Fig. 7.

DISCUSSION

Diagnosis of tumor invasion by rectal cancer plays a central role in estimating survival and determining the appropriate treatment. Survival is lower with advancing disease.

This meta-analysis and systematic review shows that the pooled sensitivity of EUS for tumor invasion (T stage) is high (approximately 88–95%), being higher for advanced

TABLE 3 Effect of EUS technology to diagnose various T stages of rectal cancers

	Year	No. of studies	Pooled sensitivity	Pooled specificity	Pooled LR+	Pooled LR–	Pooled DOR
T1	1984–1994	12	96.4% (92.3–98.7%)	98.1% (96.6–99.1%)	33.1 (9.6–114.2)	0.13 (0.07–0.21)	309.7 (116.1–826.4)
	1995–2000	14	91.4% (87.7–94.3%)	99.3% (98.5–99.7%)	57.6 (8.9–371.2)	0.12 (0.08–0.25)	443.0 (102.7–1910.7)
	2001–2008	13	79.6% (74.6–84.0%)	98.0% (97.3–98.5%)	46.0 (18.2–116.2)	0.23 (0.17–0.36)	276.6 (78.1–979.4)
T2	1984–1994	14	93.8% (90.0–96.5%)	96.1% (94.2–97.5%)	20.2 (8.9–45.9)	0.14 (0.09–0.21)	197.3 (97.5–399.3)
	1995–2000	14	77.9% (71.9–83.2%)	95.6% (94.2–96.8%)	16.1 (7.4–34.9)	0.23 (0.15–0.35)	98.6 (40.5–240.2)
	2001–2008	13	75.3% (71.4–79.0%)	95.5% (94.4–96.4%)	14.8 (11.8–18.5)	0.29 (0.19–0.43)	60.9 (43.6–85.2)
T3	1984–1994	14	96.3% (94.0–97.9%)	90.4% (87.2–93.1%)	7.8 (4.8–12.8)	0.07 (0.03–0.12)	206.9 (101.9–419.7)
	1995–2000	14	96.3% (94.3–97.8%)	92.2% (90.1–94.0%)	10.9 (5.7–20.7)	0.07 (0.03–0.16)	198.9 (68.5–577.9)
	2001–2008	13	96.5% (94.9–97.7%)	89.9% (88.2–91.4%)	8.8 (6.0–12.9)	0.05 (0.03–0.08)	220.9 (90.3–540.6)
T4	1984–1994	13	96.6% (92.1–98.9%)	98.0% (96.6–99.0%)	34.6 (10.2–116.9)	0.15 (0.08–0.25)	306.5 (113.4–828.3)
	1995–2000	11	93.8% (86.0–97.9%)	97.5% (96.2–98.5%)	28.2 (8.8–90.8)	0.17 (0.09–0.35)	263.1 (45.5–1520.5)
	2001–2008	10	95.1% (87.8–98.6%)	98.6% (98.0–99.1%)	61.7 (23.9–158.7)	0.11 (0.03–0.42)	877.8 (285.5–2698.8)

LR+, positive likelihood ratio; LR–, negative likelihood ratio; *DOR*, diagnostic odds ratio

disease than for early disease. For all the T stages, pooled specificity of EUS to diagnose depth of tumor invasion is very high (approximately 99%).

Diagnostic odds ratio is defined as the odds of having a positive test in patients with a true histological stage of the disease when compared with patients who do not have the disease. EUS as a staging test has a very high diagnostic odds ratio for T staging (about 92–360 times); for example, if EUS demonstrates that a patient has T1 stage disease, the odds of having the correct histological stage of T1 disease is 234 times. This helps physicians offer surgical treatment alone with confidence to patients with early disease. In other words, if a small rectal lesion is found to be malignant, EUS is an excellent diagnostic test to examine the depth of tumor invasion, because of its very high sensitivity and specificity. The depth of tumor invasion can help decide if curative surgery alone should be offered.

Positive likelihood ratio of a diagnostic test is a measure of how well the test correctly identifies a disease stage. The higher the positive likelihood ratio, the better the diagnostic test performs in correctly identifying the true disease state. On the flip side, the negative likelihood ratio of a diagnostic test is a measure of how well the test correctly excludes a disease stage. The lower the negative likelihood ratio, the better the diagnostic test's ability to exclude a disease stage. For T staging, EUS has a high positive likelihood ratio for all T stages and a low negative likelihood ratio. This indicates that EUS performs better in excluding as well as diagnosing the correct histological stage of rectal cancers. This helps physicians offer treatments with confidence based on EUS staging of rectal cancer.

EUS technologies, quality of imaging, and endoscopic skills have improved over the past two decades. To assess the effect of these parameters, T staging studies were grouped into periods of time. The hypothesis is that, during a period of time, the EUS technology used might be similar. The weakness of doing this kind of pooling is that some of the studies might use older technology though the paper was published in the most recent time period. However, statistically there is no alternative way of looking at this effect and this seems to be an accepted method of looking at the potential impact of technology.[34–36] Over the past two decades, the sensitivity and specificity of EUS to T-stage rectal cancers has remained the same. The specificity of EUS remained high over the past two decades. For T1 and T2 the sensitivity seemed to decrease over the past

TABLE 4 Bias indicators and AUC with corresponding Q values for various cancer stages

	Begg–Mazumdar bias (Kendall's tau value, p)	Harbord–Egger bias (95% CI, p)	AUC (SE)	Q (SE)
T1	–0.05, $p = 0.69$	−1.00 (95% CI = −2.25 to 0.24, $p = 0.15$)	0.97 (0.01)	0.92 (0.02)
T2	−0.14, $p = 0.22$	−1.78 (95% CI = −3.81 to 0.25, $p = 0.12$)	0.96 (0.01)	0.91 (0.01)
T3	0.05, $p = 0.65$	−1.25 (95% CI = −3.51 to 1.01, $p = 0.31$)	0.98 (0.01)	0.93 (0.01)
T4	−0.04, $p = 0.79$	−3.11 (95% CI = −4.82 to −1.41, $p = 0.02$)	0.98 (0.01)	0.94 (0.01)

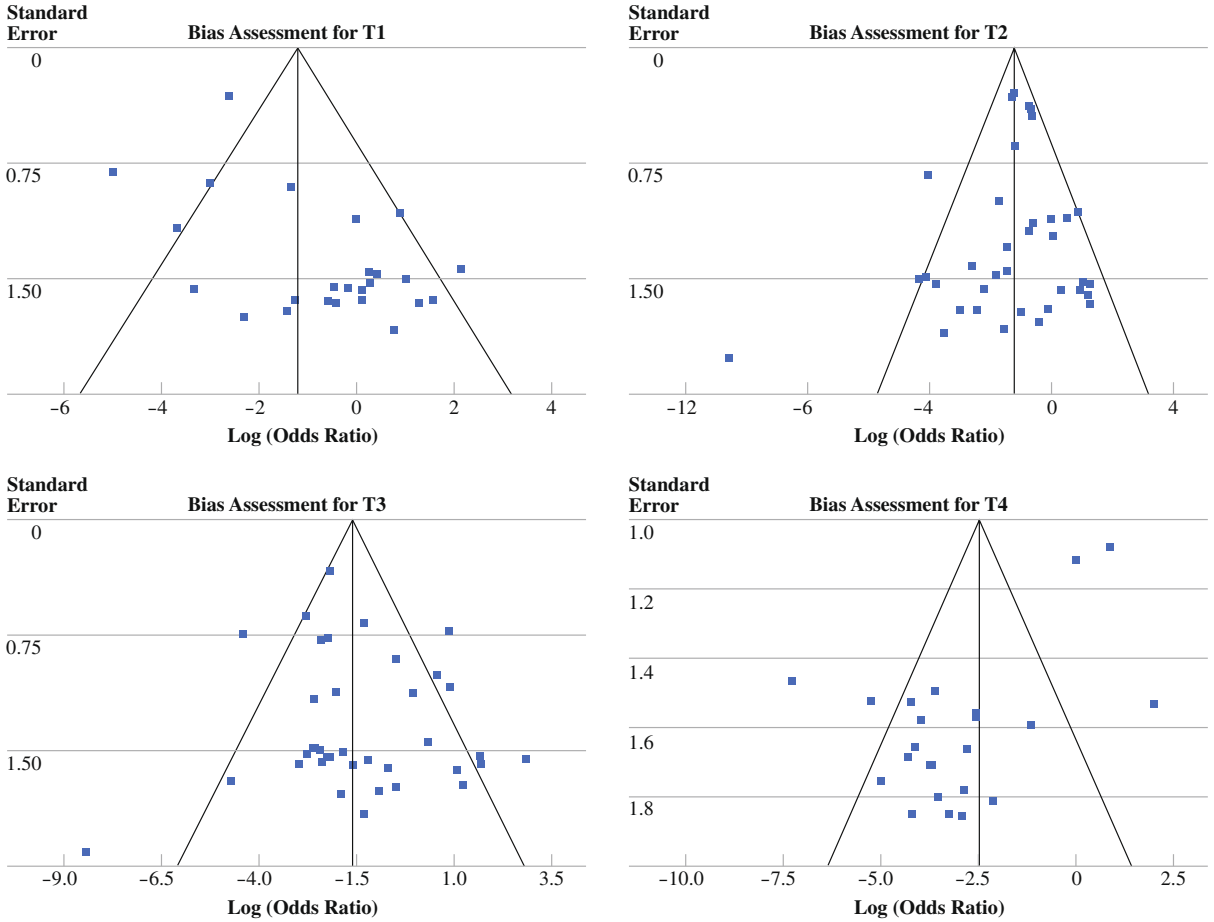

FIG. 6 Funnel plots assessing bias for T staging

two decades. This might be due to the number of studies being lower in the most recent period of time.

Heterogeneity among different studies was evaluated not only with test of heterogeneity but also by drawing SROC curves and finding the AUC, since different studies might use slightly different criteria for staging. An AUC of 1 for any diagnostic test indicates that the test is highly accurate. SROC curves for EUS showed that the AUC value was very close to 1, indicating that EUS is an excellent staging test for rectal cancers.

The majority of the studies included in this analysis were either retrospective or consecutive. QUADAS criteria for the quality of studies showed that the studies fulfilled 30–35% of the 14 criteria. Some of the criteria cannot be applied to EUS studies, so there are some inherent weaknesses of using this kind of scoring system to evaluate the quality of EUS studies. Though the quality of included studies seems to be low using the QUADAS criteria, all of the studies in the literature evaluating T staging of rectal cancers had similar scores. The effect of the results of other imaging modalities on the accuracy of EUS to T-stage rectal cancer cannot be evaluated with the available literature.

EUS studies with statistically significant results tend to be published and cited. Smaller studies may show larger treatment effects due to fewer case-mix differences (e.g., patients with only early or late disease) than larger trials. This publication and selection bias may affect the summary estimates. This bias can be estimated by bias indicators and construction of funnel plots. Bias among studies can affect the shape of the funnel plot. In this meta-analysis and systematic review, bias calculations using Harbord–Egger bias indicator and Begg–Mazumdar bias indicator showed no statistically significant bias.[41,42] Furthermore, analysis using funnel plots showed no significant publication bias among the studies included in this analysis.

CONCLUSIONS

As a result of high sensitivity and specificity, EUS can accurately stage rectal cancers. The sensitivity of EUS is higher for advanced disease than for early disease. EUS

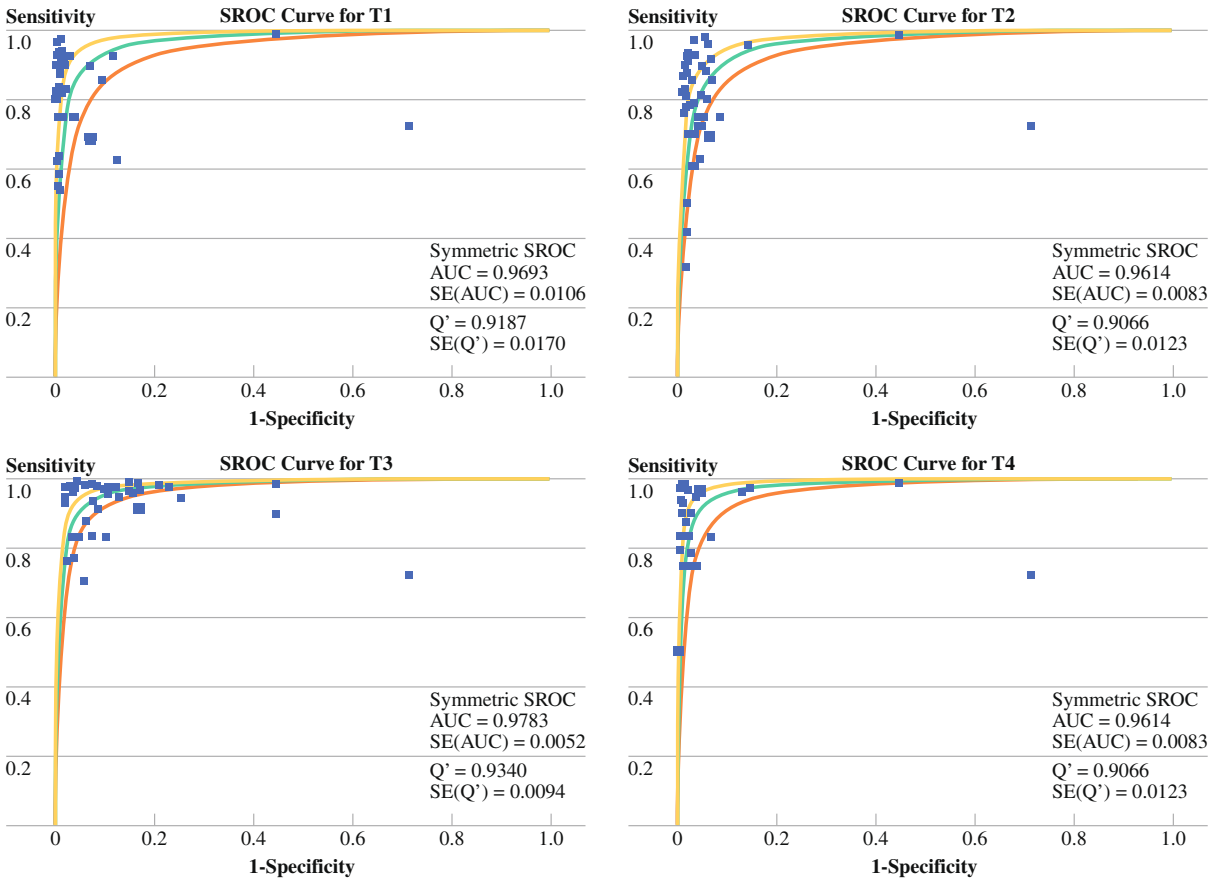

FIG. 7 SROC curves for various T stages of rectal cancer

should be strongly considered as the preferred test for providing tumor staging of rectal cancer.

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