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Diagnostic accuracy of bowel ultrasonography in patients with inflammatory bowel disease: a systematic review and meta-analysis

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Abstract

Background Bowel ultrasonography (BUS) is emerging as a promising noninvasive tool for assessing disease activity in inflammatory bowel disease (IBD) patients. We evaluated the diagnostic accuracy of BUS in IBD patients against the gold standard diagnostic method, standard colonoscopy.

Methods Major databases were searched from inception to May 2023 for studies on BUS diagnostic accuracy in IBD. Outcomes of interest were pooled sensitivity, specificity, positive (PPV), and negative (NPV) predictive values. Endoscopic confirmation served as ground truth. Standard meta-analysis methods with a random-effects model and I^2 statistics were applied. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies-2 tool.

Results Twenty studies (1094 patients) were included in the final analysis. The majority (75%) of studies considered bowel wall thickness >3 mm as abnormal. Endoscopic evaluation was performed between days 3 and 180. The pooled diagnostic accuracy of BUS in IBD was 66% (95% confidence interval [CI] 58-72%; I^2=78%), sensitivity was 88.6% (95%CI 85-91%; I^2=77%), and specificity 86% (95%CI 81-90%; I^2=95%). PPV and NPV were 94% (95%CI 93-96%; I^2=25%) and 74% (95%CI 66-80%; I^2=95%), respectively. On subgroup analysis, small-intestine contrast-enhanced ultrasonography (SICUS) demonstrated high sensitivity (97%, 95%CI 91-99%; I^2=83%), whereas BUS exhibited high specificity (94%, 95%CI 92-96%; I^2=0%) and NPV (76%, 95%CI 68-83%; I^2=80.9%). Meta-regression revealed a significant relation between side-to-side anastomosis and BUS specificity (P=0.02) and NPV (P=0.004).

Conclusion The high diagnostic accuracy of BUS in detecting bowel wall inflammation suggests utilizing regular BUS as the primary modality, with subsequent consideration of SICUS if clinically warranted.

Keywords Bowel ultrasound, inflammatory bowel disease, meta-analysis

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Introduction

Inflammatory bowel disease (IBD), including ulcerative colitis (UC), and Crohn's disease (CD), is known to cause recurring episodes of inflammation in the gastrointestinal tract, significantly impacting the quality of life of affected individuals [1]. Along with endoscopic and histological healing, achieving and maintaining clinical remission is critical for the effective management of IBD [2].

Regular monitoring of IBD patients is necessary to maintain symptom stability and proactively prevent disease flares. This involves a combination of clinical symptom assessment, measurement of fecal calprotectin and/or high-

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sensitivity C-reactive protein levels, and periodic colonoscopy exams [3]. In recent years, we have seen emerging data on the use of bedside bowel ultrasound (BUS) in assessing disease activity in patients with IBD. Office-based BUS seems to hold promise as a noninvasive, convenient, and cost-effective method of monitoring disease activity [4,5].

Changes in bowel wall thickness are used as a marker of inflammation in BUS, and complications such as abscesses or strictures can also be identified [6]. Furthermore, BUS allows for real-time evaluation, making it a useful tool for guiding treatment decisions and monitoring responses to therapy [7,8]. However, despite its potential as a noninvasive tool for evaluating inflammation in patients with IBD, the diagnostic accuracy of BUS has not been extensively validated by meta-analysis. In this study, we aimed to evaluate the pooled diagnostic accuracy of BUS in patients with IBD.

Materials and methods

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (PRISMA checklist provided in the supplementary material: Appendix 1) [9].

Search strategy

We conducted a comprehensive search of several databases and conference proceedings, including the PubMed, Ovid, Cochrane and CINHAL databases (earliest inception to May 2023). An experienced medical librarian using inputs from the study authors helped with the literature search to identify studies reporting BUS in patients with IBD. The detailed literature search strategy is provided in Appendix 2. Two authors (SM, SV) independently reviewed the titles and abstracts of studies identified in the primary search and excluded studies that did not address the research question, based on prespecified exclusion and inclusion criteria. The full text of the remaining articles was reviewed to determine whether it contained relevant information. Any discrepancy in article selection was resolved by consensus, and in discussion with a co-author (BPM). The bibliographic section of the selected articles, as well as the systematic and narrative articles on the topic, were manually searched for additional relevant articles.

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Study selection

In this meta-analysis, we included studies that reported on the clinical and technical outcomes of BUS in patients with IBD and met the following criteria: 1) evaluation of BUS in patients with IBD; and 2) specific information provided on diagnostic accuracy parameters of BUS in assessing IBD disease activity, including IBD flare and postoperative CD recurrence. Studies were included irrespectively of the geography and abstract/manuscript status, as long as they provided the data needed for our analysis. We excluded studies that did not provide sufficient data to allow estimation of outcomes of interest. The standard procedure used as a control was colonoscopy/ileocolonoscopy. Details are provided in Supplementary Table 1. In the case of multiple publications from the same cohort, data from the most recent comprehensive report were included.

Data abstraction and quality assessment

Data on study-related outcomes in the individual studies were abstracted into a standardized form by 2 authors (SV, BT) independently. Assessment of risk of bias in the included studies was carried out using the Quality Assessment of Diagnostic Accuracy Studies - 2 (QUADAS-2) tool, and 2 authors (SM, SRK) did the quality scoring independently [10]. The details of the study quality assessment are summarized in Supplementary Table 2.

Outcomes assessed

The primary analysis of this study focused on calculating the pooled rate of diagnostic accuracy parameters of BUS in IBD, such as accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Subgroup analysis was planned to study the pooled diagnostic accuracy outcomes with standard BUS and small-intestine contrast-enhanced US (SICUS), for CD and UC.

Statistical analysis

We used meta-analysis techniques to calculate the pooled estimate in each case, following the methods suggested by DerSimonian and Laird [11] and using the random-effects model, and our application can be seen to fit within their general approach (where the effect is measured by probability of risk). When the incidence of an outcome was 0 in a study, a correction of 0.01 was added to the number of incident cases before statistical analysis [12]. We assessed heterogeneity

between study-specific estimates using 2 methods: Cochrane Q statistics and I^2 statistics. [13,14] Values of <30%, 30-60%, 61-75%, and >75% were suggestive of low, moderate, substantial and considerable heterogeneity, respectively [15]. Publication bias was ascertained qualitatively, by visual inspection of the funnel plot, and quantitatively, by the Egger test [16]. All analyses were performed using Comprehensive Meta-Analysis (CMA) software, version 4 (BioStat, Englewood, NJ).

Results

Search results and population characteristics

From a total of 487 citations identified by our literature search, 427 titles were screened and 45 full-length articles were assessed for eligibility. Of these, 20 studies were included in the final meta-analysis [17-36]. The schematic diagram of the study selection is illustrated in Fig. 1.

Table 1 describes the population characteristics. A total of 1094 patients were studied. The majority of the patient population were male (66.67%), and the mean age was 40.17 (14-54) years.

Characteristics and quality of included studies

Table 1 describes the characteristics of the included studies. The meta-analysis included 20 independent cohort studies, with a total of 1094 patients: 5 studies (n=291) assessed UC patients, while 15 studies (n=803) assessed the use of BUS in patients with CD, 10 studies in postoperative recurrence of CD (n=436), 2 CD in general (n=181) and 3 in both CD and postoperative CD combined (n=186).

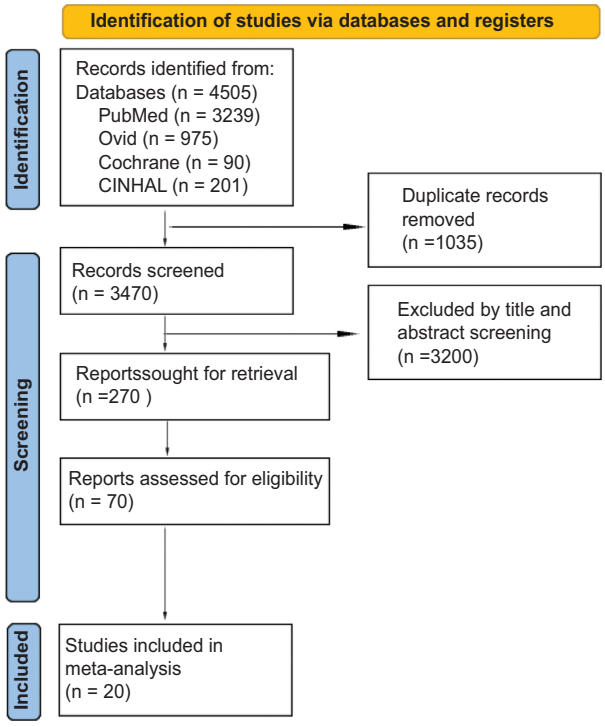

Figure 1 PRISMA study selection flow chart

The sonographic examinations were carried out using a convex or linear 2-16 MHz probe. The number of operators varied from 1-6. For the majority (75%) of the studies, a bowel wall thickness >3 mm was considered abnormal. The other parameters assessed for activity on intestinal ultrasound are summarized in Supplementary Table 3. The lag time (time interval between US and endoscopy) was reported in 17 studies. The mean lag time was 22 (range: 3-180) days.

None of the studies were population-based. Only 1 study (Ripolles *et al*, 2021) was multicenter-based, whereas the rest were single-center. All studies reported clear information regarding the diagnostic accuracy parameters of BUS in IBD: accuracy, sensitivity, specificity, PPV, and NPV. All the studies included were original manuscripts. Supplementary Table 1 provides details of the study quality assessment.

Meta-analysis outcomes

Cumulative pooled rates

The cumulative pooled rate for the diagnostic accuracy of BUS in IBD was 66% (95% confidence interval [CI] 58-72%; I^2=78%). The cumulative pooled rate of sensitivity was 88.6% (95%CI 85-91%; I^2=77%) (Forest plot, Fig. 2), while the specificity was 86% (95%CI 81-90%; I^2=95%) (Forest plot, Fig. 3). The pooled rates of PPV and NPV were 94% (95%CI 93-96%; I^2=25%), and 74% (95%CI 66-80%; I^2=95%), respectively.

Pooled rates based on BUS, BUS with color Doppler, and SICUS

A subgroup analysis was performed to study the accuracy outcomes of standard BUS, SICUS, and color Doppler BUS in IBD. SICUS demonstrated high sensitivity (97%, 95%CI 91-99%; I^2=83%), whereas BUS exhibited high specificity (94%, 95%CI 92-96%; I^2=0%), and NPV (76%, 95%CI 68-83%; I^2=80.9%).

Pooled rates in CD, postoperative CD recurrence, and UC

A subgroup analysis was conducted based on IBD subtypes to study the outcomes of BUS in CD, postoperative CD recurrence, and UC. The pooled NPV for postoperative CD recurrence was noted to be low at 53% (95%CI 32-72%; I^2=95%).

Pooled rates of BS, BS with color Doppler and SICUS in CD

We additionally performed a subgroup analysis to study the pooled diagnostic accuracy of various BUS subtypes exclusively in CD, which included CD and postoperative recurrence of

Table 1 Study and population characteristics

First author, year [ref.]	Study type, center, time frame, country	IBD type (UC or CD or post-op CD)	Total patients	Sex (m/f)	Mean age	Lag time (interval between US and endoscopy)
Andreoli, 1998 [17]	Prospective observational, single-center, 1992-1996, Rome, Italy	Post-op CD	41	26/15	42.4	14 days
Allocca, 2021 [18]	Prospective observational study, single-center (tertiary), May 2019-May 2020, Milan, Italy	UC	43	27/16	39.01 at diagnosis, 53.81 at inclusion	7 days
Biancone, 2007 [19]	Prospective observational study, single-center (tertiary), January 2004-April 2005, Rome, Italy	Post-op CD	22	12/10	38.5	-
Bots, 2021 [20]	Prospective observational study, single-center, Norway	UC	60	28/32	44	21 days
Calabrese, 2009 [21]	Prospective observational study, single-center (tertiary), May 2004-April 2008, Rome, Italy	Post-op CD	72	34/38	44	6 months
Castiglione, 2008 [22]	Prospective observational study, single-center, January 2005-February 2007, Naples, Italy	Post-op CD	40	22/18	38	7 days
Lalosevic, 2022 [23]	Retrospective study, single-center, November 2019-January 2022, Serbia	UC	55	33/22	44.2	-
Onali, 2010 [24]	Prospective observational study, single-center (tertiary), July 2003-April 2005, Rome, Italy	Post-op CD	25	14/11	36.48	-
Onali, 2016 [25]	Prospective observational study, single-center (tertiary), July 2003-February 2007, Rome, Italy	Post-op CD	40	23/17	39	-
Pallotta, 2010 [26]	Prospective observational study, single-center, 2000-, Rome, Italy	Post-op CD	58	37/21	45.4	14 days
Ponorac, 2023 [27]	Prospective study, single-center, January 2018-March 2019, Slovenia	CD	36 children	15/21	14	30 days
Paredes, 2010 [28]	Prospective study, single-center, January 2006-May 2007, Valencia, Spain	Post-op CD	33	22/11	41.2	3 days
Paredes, 2013 [29]	Prospective study, single-center, January 2007-December 2010, Valencia, Spain	Post-op CD	60	32/28	39	3 days
Ramaswamy, 2020 [30]	Prospective study, single-center, July 2017-July 2018, India	CD and Post-op CD	35	19/16	33-34	14 days
Rispo, 2006 [31]	Prospective study, single-center, March 2002-October 2005, Naples, Italy	Post-op CD	45	25/20	37	7 days

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Table 1 (*Continued*)

First author, year [ref.]	Study type, center, time frame, country	IBD type (UC or CD or post-op CD)	Total patients	Sex (m/f)	Mean age	Lag time (interval between US and endoscopy)
Ripolles, 2021 [32]	Prospective observational study, multicenter, January 2017-December 2018, Madrid, Spain	CD and Post-op CD	72	36/36	36.5 at diagnosis, 45.6 at study	30 days
Sagami, 2020 [33]	Cross sectional study, single-center, August 2018-March 2019, Tokyo, Japan	UC	53	40/13	41	7 days
Saevik, 2020 [34]	Cross sectional study, single-center, 2015-2019, Norway	CD	145	58/87	42 active 38 remission group	14 days
Takahara, 2021 [35]	Prospective study, single-center, 2016-December 2019, Okayama, Japan	UC	80	56/24	51	14 days
Yigit, 2022 [36]	Prospective study, single-center, May 2018-June 2019, Turkey	CD and Post-op CD	79	57/22	37.5	7 days

IBD, inflammatory bowel disease; UC, ulcerative colitis; CD, Crohn's disease; US, ultrasound

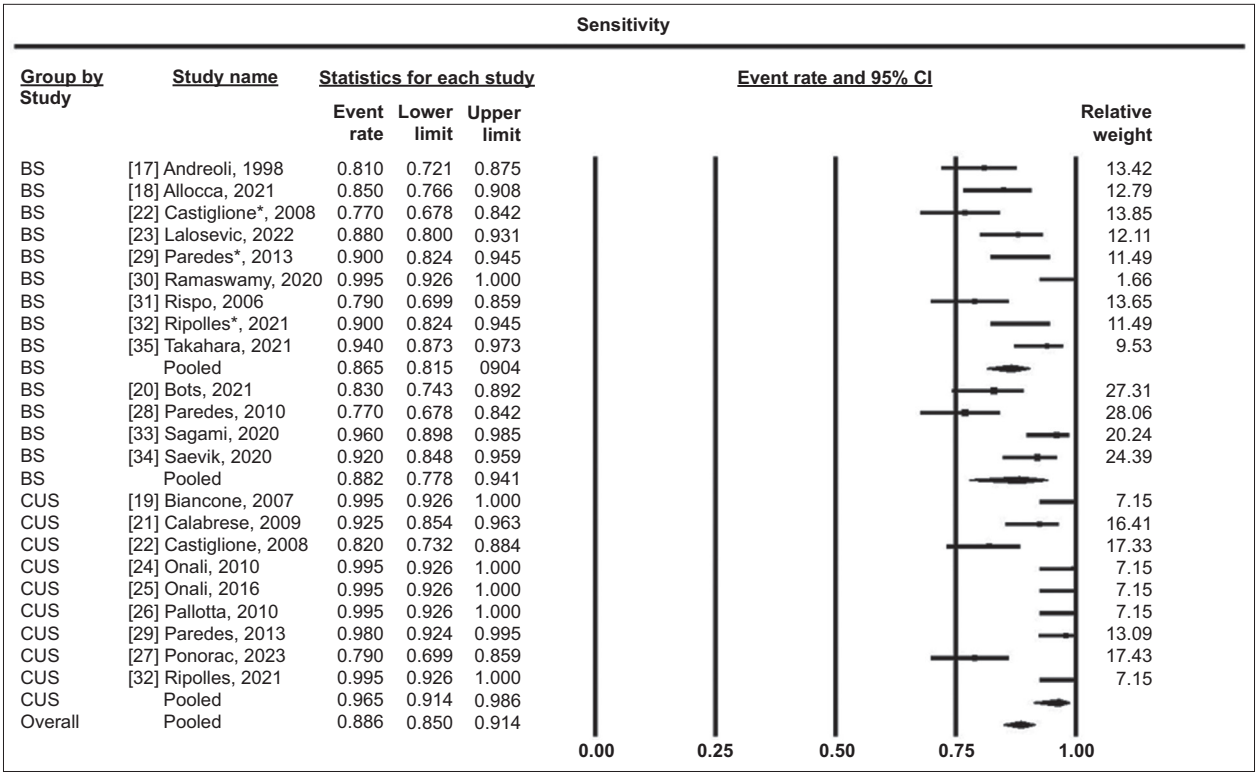

Figure 2 Forest plot, sensitivity of BUS in IBD: overall and by BUS subtypes
BUS, bowel ultrasound; IBD, inflammatory bowel disease; CI, confidence interval

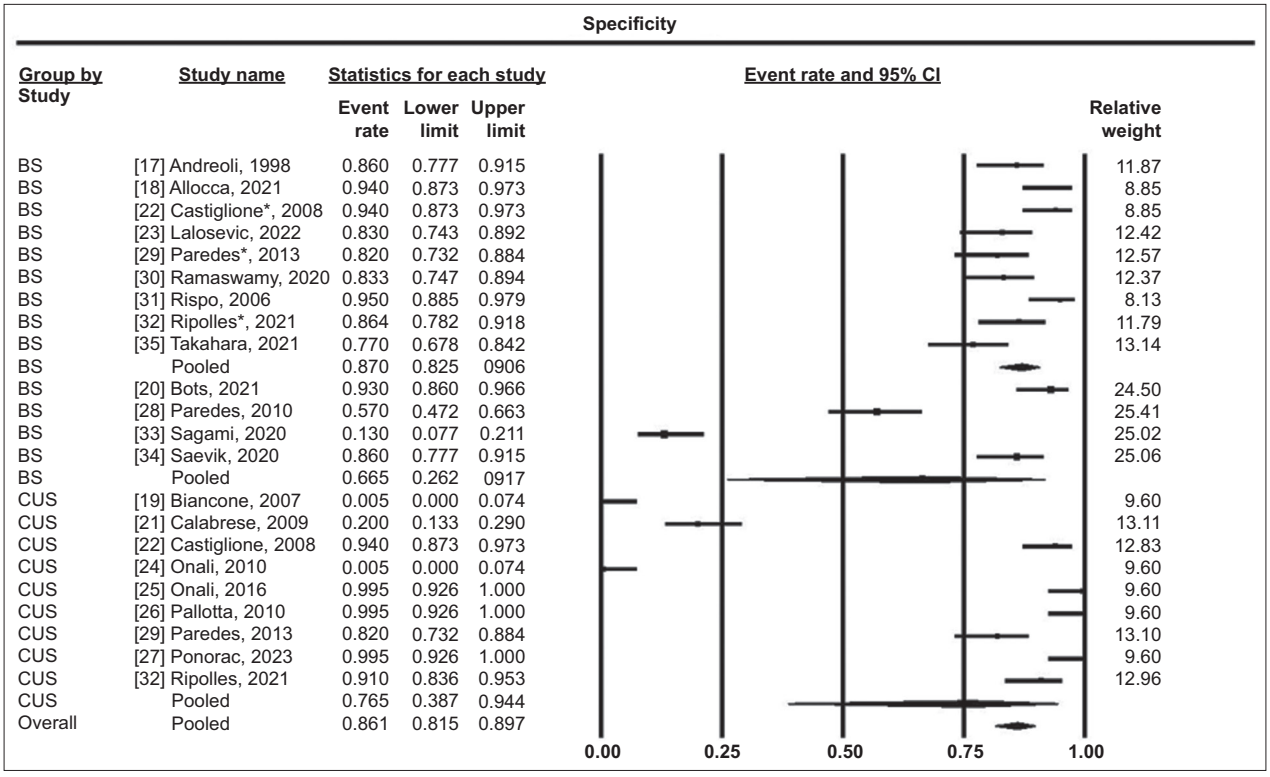

Figure 3 Forest plot, specificity of BUS in IBD: overall and by BUS subtypes
BUS, bowel ultrasound; IBD, inflammatory bowel disease; CI, confidence interval

CD. BUS, BUS with color Doppler and SICUS demonstrated excellent sensitivity and PPV. The NPV for SICUS was noted to be low at 50% (95%CI 20-80%; I^2=96%).

Meta-regression analysis by anastomosis types in postoperative CD recurrence

A meta-regression analysis was conducted to ascertain if the type of anastomosis in postoperative CD affected the pooled outcomes. In particular, end-to-side anastomosis demonstrated a significant correlation with PPV (P=0.04), while side-to-side anastomosis seemed to demonstrate a significant correlation with specificity (P=0.02) and NPV (P=0.004).

All pooled rates with corresponding I^2 heterogeneity are summarized in Table 2. Forest plots are illustrated in Supplementary Fig. 1-12.

Validation of meta-analysis results

Sensitivity analysis

To assess the possible dominant effect of individual studies on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. We did not find any single study that significantly affected the outcomes of interest or the heterogeneity.

Heterogeneity

Since pooled diagnostic accuracy parameters were evaluated in this study, the statistical concept of heterogeneity does not apply here. Nevertheless, we have reported the I^2 values for all pooled outcomes studied in Table 2, alongside the pooled rates. A high heterogeneity was expected because of variability in BUS technique, BUS subtypes, and IBD subtypes.

Publication bias

A publication bias assessment was deferred in this study as the concept of "sample size" to "effects size" does not apply to diagnostic accuracy studies.

Discussion

Our study, in contrast to those of Rispo *et al* and Shintaro Sagami *et al* [37,38], assessed BUS in a broader context, including CD, postoperative CD recurrence, and UC. We also analyzed various BUS subtypes for CD, and our meta-regression explored the impact of different anastomotic surgeries on postoperative CD. This meta-analysis of 20 studies evaluating BUS in patients with IBD demonstrated excellent pooled rates of diagnostic accuracy.

Table 2 Cumulative diagnostic accuracy parameters of bowel US in IBD and based on US subtypes

Outcomes	Pooled rate (95% confidence interval)	I^2 heterogeneity
Cumulative diagnostic accuracy parameters of bowel US in IBD and based on US subtypes		
Positive ultrasound	66% (58-72%); 17 studies	78%
BUS	60% (48-71%); 6 studies	71%
BUS with US color Doppler	63% (52-74%); 3 studies	66%
SICUS	80% (69-90%); 8 studies	82%
Sensitivity	88.6% (85-91%); 22 studies	77%
BUS	87% (82-90%); 9 studies	69%
BUS with US color Doppler	88% (78-94%); 4 studies	82%
SICUS	97% (91-99%); 9 studies	83%
Specificity	86% (81-90%); 22 studies	95%
BUS	87% (82-90%); 9 studies	68%
BUS with US color Doppler	67% (26-91%); 4 studies	97%
SICUS	76% (39-94%); 9 studies	96%
Positive predictive value	94% (93-96%); 19 studies	25%
BUS	94% (92-96%); 8 studies	0%
BUS with US color Doppler	90% (81-96%); 2 studies	63%
SICUS	96% (94-97%); 9 studies	17%
Negative predictive value	74% (66-80%); 19 studies	95%
BUS	76% (68-83%); 8 studies	81%
BUS with US color Doppler	63% (21-91%); 2 studies	97%
SICUS	50% (20-80%); 9 studies	96%
Diagnostic accuracy parameters of BUS in IBD subtypes		
Sensitivity:		
CD and postoperative CD	92% (83-97%); 5 studies	80%
Postoperative CD	90% (84-94%); 12 studies	79%
UC	89% (84-93%); 5 studies	66%
Overall	90% (87-93%); 22 studies	77%
Specificity:		
CD and postoperative CD	87% (81-91%); 5 studies	53%
Postoperative CD	76% (54-90%); 12 studies	95%
UC	77% (42-94%); 5 studies	97%
Overall	86% (80-90%); 22 studies	95%
Positive predictive value:		
CD and postoperative CD	94% (91-96%); 5 studies	13%
Postoperative CD	95% (92-96%); 12 studies	40%
UC	94% (90-97%); 2 studies	0%
Overall	94% (93-96%); 19 studies	25%
Negative predictive value:		
CD and postoperative CD	81% (67-90%); 5 studies	89%
Postoperative CD	53% (32-72%); 12 studies	95%
UC	80% (73-84%); 2 studies	0%
Overall	77% (71-82%); 19 studies	95%
Diagnostic accuracy parameters of BUS subtypes in Crohn's disease patients and post-op recurrence of Crohn's disease		
Positive ultrasound, overall	67% (59-74%); 16 studies	78%
BUS	61% (49-74%); 5 studies	76%
BUS with US color Doppler	64% (52-74%); 3 studies	66%
SICUS	67% (59-74%); 8 studies	82%
Sensitivity, overall	90% (85-93%); 16 studies	80%
BUS	87% (78-92%); 5 studies	75%
BUS with US color Doppler	86% (64-95%); 2 studies	87%
SICUS	96% (91-98%); 9 studies	83%
Specificity, overall	85% (80-89%); 16 studies	94%
BUS	86% (81-89%); 5 studies	42%
BUS with US color Doppler	74% (39-92%); 2 studies	95%
SICUS	76% (39-95%); 9 Studies	96%

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Table 2 (*Continued*)

Outcomes	Pooled rate (95% confidence interval)	I^2 heterogeneity
Positive predictive value, overall	95% (93-96%); 16 studies	34%
BUS	94% (91-96%); 5 studies	0%
BUS with US color Doppler	90% (81-96%); 2 studies	63%
SICUS	96% (94-97%); 9 studies	17%
Negative predictive value, overall	70% (57-80%); 16 studies	95%
BUS	75% (60-85%); 5 studies	86%
BUS with US color Doppler	63% (20-91%); 2 studies	97%
SICUS	50% (20-80%); 9 studies	96%
Meta-regression (by surgical anastomosis type)		
Anastomosis subtype	Knapp-Hartung 2-tailed P-value Positive US; sensitivity; specificity; PPV; NPV	
End-to-end	0.7; 0.9; 0.6; 0.4; 0.8	
Side-to-end	0.6; 0.8; 0.9; 0.4; 0.7	
End-to-side	0.5; 0.4; 0.6; 0.04; 0.1	
Side-to-side	0.1; 0.9; 0.02; 0.7; 0.004	

BUS, bowel ultrasound; US, ultrasound; SICUS, small intestine contrast ultrasound; IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; PPV, positive predictive value; NPV, negative predictive value

The overall cumulative sensitivity was 88.6%, specificity was 86%, PPV was 94% and NPV was 74%. Additionally, we performed an analysis based on BUS subtypes (such as BUS, BUS with color Doppler, SICUS) and IBD subtypes (CD, postoperative CD, UC). Excellent sensitivity and PPV were demonstrated with each BUS subtype, especially with SICUS. Similarly, excellent sensitivity and PPV were noted with each IBD subtype. To the best of our knowledge, this is the largest pooled quantitative synthesis of diagnostic parameters of BUS in patients with IBD.

BUS is a cost-effective and easy-to-use bedside modality that can provide immediate outpatient clinical data to the gastroenterologist if an IBD flare is suspected in an office-based setting. Furthermore, inpatient resources and time could be potentially saved. Although excellent diagnostic accuracy parameters are demonstrated in this study, the most appropriate BUS tool is currently unknown. We observed a sensitivity of 97% and a PPV of 96% with SICUS; however, the NPV was only 50%. On the other hand, regular BUS demonstrated a sensitivity of 87%, a PPV of 87%, a specificity of 87% and an NPV of 74%. The reported values seem to suggest that regular BUS could be the first-line ultrasound modality in patients with IBD, and SICUS could be a second-line modality for further detailed examinations if clinically warranted. Previous studies have shown a correlation between the qualitative evaluation of SICUS and IBD clinical activity [39-42].

In terms of IBD subtypes, the sensitivity of BUS in CD and postoperative CD combined was 92%, PPV was 94%, specificity was 87% and NPV was 81%. For UC, BUS demonstrated a sensitivity of 89%, a PPV of 94%, a specificity of 77% and an NPV of 80%. These values suggest that BUS demonstrated good diagnostic accuracy values in both CD and UC. However, the UC findings were limited to fewer studies. In patients with CD and postoperative recurrence of CD, SICUS demonstrated a sensitivity and PPV of 96%, though with an NPV of only 50%. Therefore, as stated above, regular BUS could be an appropriate first-line modality, followed by intestinal contrast enhancement if clinically warranted. Data categorized by BUS subtypes were not available for patients with UC. It is worth noting that the existing literature on BUS primarily focuses on its use in CD rather than UC, underscoring the need for more studies in UC patients. Regardless of the type of IBD, a wall thickness of >3 mm was used as the cutoff in the majority of the studies to diagnose a potential inflammation of the bowel wall.

Our meta-regression analysis of various types of anastomotic surgeries in the context of BUS in postoperative CD yielded interesting results. End-to-end, side-to-end, end-to-side and side-to-side anastomoses were assessed for any potential effects on diagnostic accuracy results with BUS in postoperative CD. Although the majority of the parameters were not affected by the type of anastomoses, PPV seemed to have significant association with end-to-side anastomosis, while side-to-side anastomosis seemed to have a significant association with BUS specificity and NPV. Theoretically, one could hypothesize that a side-to-side anastomosis would display a much thicker bowel wall in the presence of inflammation; conversely, a higher NPV could be anticipated in the absence of inflammation. This is a unique finding of this study. However, previous studies have reported variability in this regard, with some reporting no influence of the type of surgical anastomosis on bowel sonography outcomes [22,24]. On the same note, it is important to state that meta-regression analysis is a weak statistical tool and further studies are warranted to establish this finding.

The strengths of this review lie in the systematic literature search with well-defined inclusion criteria, careful exclusion of irrelevant and redundant studies, the inclusion of high-quality studies with detailed extraction of data, and statistics to establish and/or refute the validity of the results of our meta-analysis. Our study is applicable to a broad and diverse clinical setting, with important findings that suggest the utilization of BUS in IBD. This study also had limitations. There was inherent heterogeneity between the different studies in

our analysis, owing to the various BUS modalities studied, IBD subtypes and technical differences. Many patient characteristics and clinical symptoms were unaccounted for and might have contributed to the observed heterogeneity. The lag time between BUS exam and confirmatory endoscopy varied widely. While a separate postoperative CD analysis would have been beneficial, it was unfeasible in view of the unsegregated data in the original studies. Our primary aim was to assess the diagnostic accuracy of ultrasound in IBD, leaving real-life studies to address the clinical implications of these findings. Despite these limitations, our study provides valuable information on the pooled diagnostic accuracy of BUS in IBD. The pooled parameters classified by BUS and IBD subtypes are key findings of this study. Furthermore, the meta-regression analysis demonstrating an excellent NPV of BUS in side-to-side anastomosis is a unique finding.

In conclusion, based on this meta-analysis, excellent pooled diagnostic parameters were demonstrated with BUS in patients with IBD. Regular office-based BUS could be the first-line modality, followed by SICUS if clinically warranted. The majority of current data relate to patients with CD and postoperative recurrence of CD, warranting future studies in patients with UC. BUS seemed to yield a good NPV in postoperative CD patients with side-side anastomosis. Future prospective studies are warranted to establish the role of BUS in patients with IBD.

Summary Box

What is already known:

- Regular monitoring of patients with inflammatory bowel disease (IBD) is vital for maintaining symptom stability and preventing disease flares
- Bowel ultrasound (BUS) is a real-time evaluation tool used for treatment guidance and therapy monitoring in IBD patients

What the new findings are:

- Excellent diagnostic accuracy was observed with BUS in patients with IBD, particularly when a cutoff of 3 mm or greater was used to diagnose bowel wall inflammation
- Small intestine contrast-enhanced ultrasonography (SICUS) exhibited high sensitivity, while BUS demonstrated remarkable specificity and negative predictive value
- Regular monitoring of IBD patients can be efficiently achieved through office-based BUS, serving as a primary diagnostic modality
- When necessary, clinicians can consider using SICUS as a follow-up diagnostic tool to complement BUS, ensuring comprehensive disease assessment and personalized care

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Supplementary material

Supplementary Table 1 Reference standard details for inflammable bowel disease activity

First author, year [ref.]	Reference Standard Type	Reference Standard Details
Andreoli, 1998 [17]	Colonoscopy	Endoscopic recurrence was defined as the presence of typical CD lesions in the neo-terminal ileum and/or anastomosis. Hyperemia alone was not considered as a sign of recurrence
Allocca, 2021 [18]	Colonoscopy	The endoscopic activity was evaluated by CS according to the MES, and mucosal healing was defined by an absolute MES of 0 or 1
Biancone, 2007 [19]	Colonoscopy or sigmoidoscopy	Endoscopic disease activity was scored using the UCEIS and the MES for each segment
Bots, 2021 [20]	Ileocolonoscopy	The degree of recurrence was assessed according to Rutgeerts' score (0–4). Endoscopic findings were documented in all patients by photographic verification
Calabrese, 2009 [21]	Conventional colonoscope	Endoscopic diagnosis and grading of PSR were made according to Rutgeerts. A grade 3 was considered indicative of severe PSR
Castiglione, 2008 [22]	Total colonoscopy	Colonoscopy findings were scored according to the MES for each segment. The extent of disease was scored according to the Montreal classification
Lalosevic, 2022 [23]	Ileocolonoscopy	Endoscopical assessment of recurrence, and the severity of recurrence assessed according to the Rutgeerts' score
Onali, 2016 [25]	Ileocolonoscopy	The severity of recurrence graded according to the Rutgeerts' score
Pallotta, 2010 [26]	Ileocolonoscopy	Presence of mucosal lesions and grading according to Rutgeerts score
Ponorac, 2023 [27]	Ileocolonoscopy	Endoscopic disease activity was determined at the time of procedure using the validated SES-CD
Paredes, 2010 [28]	Pentax EC-380 LKP 4.2 colonoscope	Severity of the lesions in the neoterminal ileum was assessed according to the Rutgeerts scale
Paredes, 2013 [29]	Not specified	The severity of the lesions in the neoterminal ileum was assessed according to the Rutgeerts scale.
Ramaswamy, 2020 [30]	Standard video endoscope	Clinical disease activity was assessed by the Harvey-Bradshaw Index. Endoscopic activity was scored by the SES-CD or by the Rutgeerts score
Rispo, 2006 [31]	Conventional colonoscope	Endoscopic diagnosis and grading of PSR were made according to Rutgeerts score
Ripolles, 2021 [32]	Ileocolonoscopy	The SES-CD was used. Endoscopic remission was considered when SES-CD was≤3 and endoscopic activity in patients with SES-CD>3. The Rutgeerts score was used for patients who had previous surgery, with a score>1 indicating active disease
Sagami, 2020 [33]	Conventional colonoscope	MES and the UCEIS
Saevik, 2020 [34]	Ileocolonoscopy	SES-CD
Takahara, 2021 [35]	Conventional colonoscope	BWT and MES
Yigit, 2022 [36]	Conventional colonoscope	Crohn's Disease Activity Index, Harvey–Bradshaw Index, and SES-CD scores

CD, Crohn's disease; CS, contrast sonograpghy; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; PSR, postsurgical recurrence; SES-CD simplified endoscopic score for CD, MES, Mayo endoscopic subscore

Supplementary Table 2 QUADAS-2 risk of bias assessment

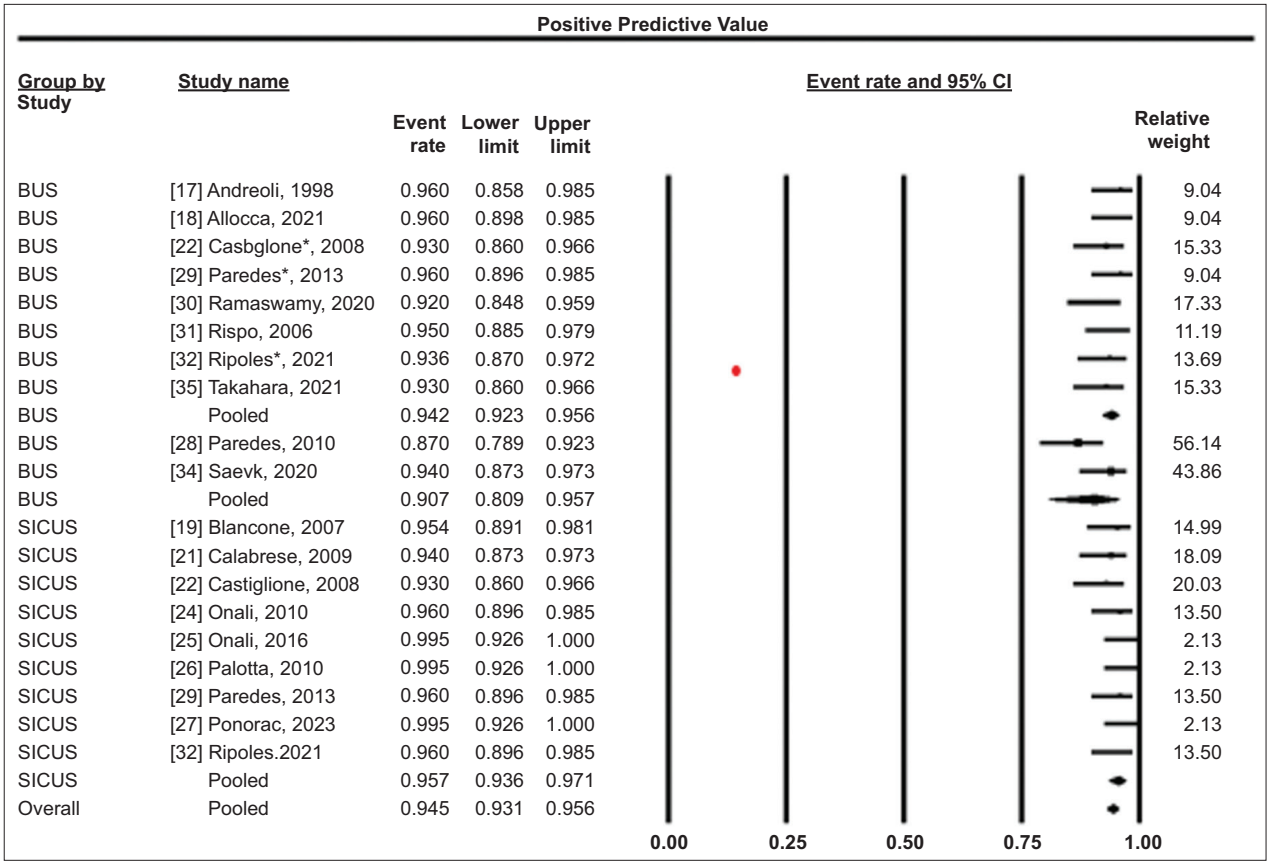
First author, year [ref.]	Risk of bias				Applicability concerns		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Andreoli, 1998 [17]	?	☺	?	☹	?	☺	☹
Allocca, 2021 [18]	?	☺	☺	?	?	?	☺
Biancone, 2007 [19]	?	☺	?	☹	?	☺	☹
Bots, 2021 [20]	?	?	☺	?	?	?	?
Calabrese, 2009 [21]	?	?	☺	?	?	?	☺
Castiglione, 2008 [22]	?	?	☺	?	?	?	☹
Lalosevic, 2022 [23]	?	☺	?	?	?	☺	☺
Onali, 2010 [24]	?	☺	☺	?	?	?	☺
Onali, 2016 [25]	?	☺	?	☹	?	☺	☹
Pallotta, 2010 [26]	?	☺	?	?	☺	☺	?
Ponorac, 2023 [27]	?	☺	☺	☹	?	☺	?
Paredes, 2010 [28]	?	☺	☺	☹	?	☺	☺
Paredes, 2013 [29]	☹	☺	☺	?	?	☺	?
Ramaswamy, 2020 [30]	?	☺	?	☹	?	☺	☹
Rispo, 2006 [31]	?	☺	?	☹	?	☺	☹
Ripolles, 2021 [32]	?	☺	?	☹	?	☺	☹
Sagami, 2020 [33]	?	?	?	☹	?	?	☹
Saevik, 2020 [34]	?	☺	?	?	?	☺	?
Takahara, 2021 [35]	?	☺	?	?	☹	☺	?
Yigit, 2022 [36]	?	☺	?	☹	?	☺	☹

☺ *low risk* ☹ *high risk* ? *unclear risk*

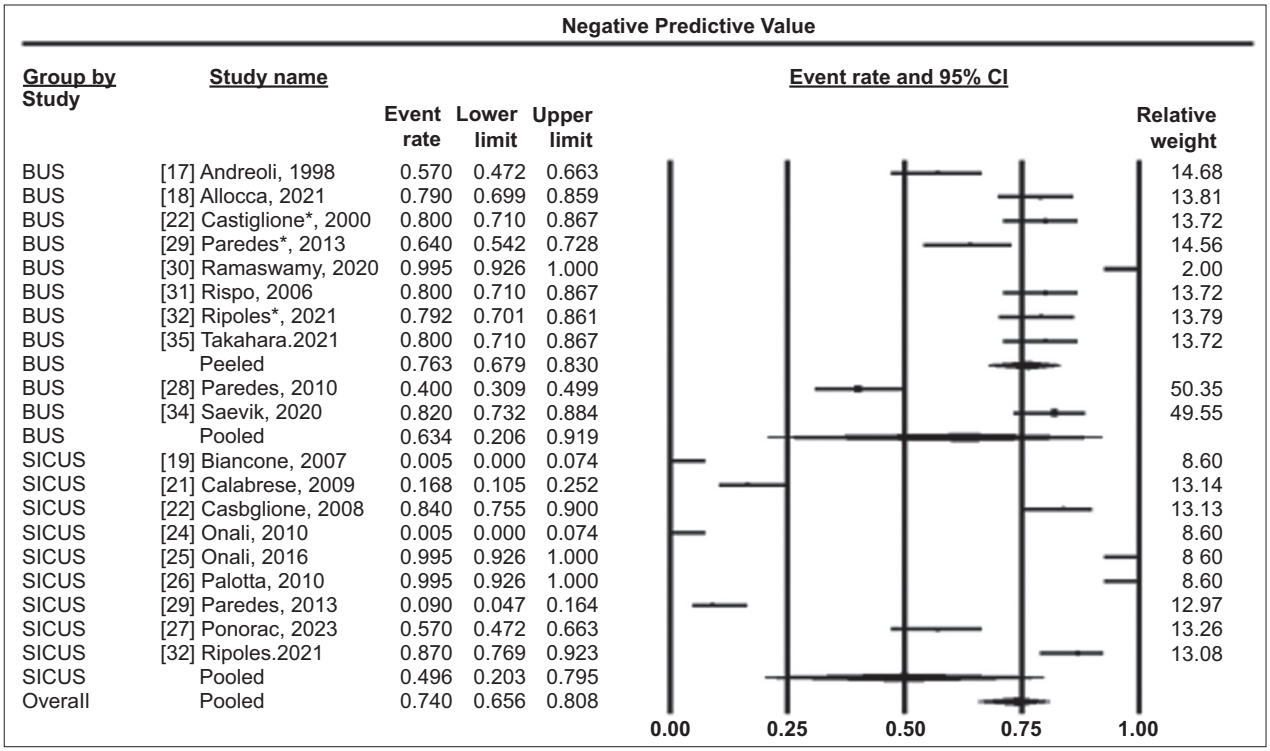
Supplementary Table 3 Parameters assessed for inflammable bowel disease activity on Ultrasonography

First author, year [ref.]	Parameters Assessed
Andreoli, 1998 [17]	- CWT - CWP - CWF- Enlarged mesenteric lymph nodes - Mesenteric hypertrophy
Allocca, 2021 [18]	- Ileal wall thickness
Biancone, 2007 [19]	- Increased BWT- "Stiff loop" - Small bowel dilation - Bowel stricture - Fistulae - Mesenteric enlargement and/or masses - Abscesses
Bots, 2021 [20]	- BWT - CDS - Image quality - Colonic haustrations - Presence of fat wrapping (hyperechoic fat around the bowel) - Wall layer stratification - Presence of enlarged lymph nodes
Calabrese, 2009 [21]	- Disease site (based on BWT) - Extent of lesions - Echo pattern - Presence of lymph nodes and/or fibrofatty proliferation - Presence of complications (stenosis, prestenotic dilation, abscess, fissures, or fistulas)
Castiglione, 2008 [22]	- Increased BWT for at least 4 cm at perianastomotic area - Small bowel dilation - Small bowel stricture - Fistulae - Mesenteric adipose tissue alteration and/or masses - Abscesses
Lalosevic, 2022 [23]	- BWT - Presence of fat wrapping - Wall layer stratification - Mesenteric hypertrophy - Presence of enlarged mesenteric lymph nodes - Absence or presence of ascites
Onali, 2010 [24]	- Increased BWT - "Stiff loop" - Small bowel dilation - Bowel stricture - Fistulae - Mesenteric enlargement and/or masses - Abscesses
Pallotta, 2010 [26]	- Increased BWT - Bowel stenosis - Bowel dilatation
Ponorac, 2023 [27]	- BWT
Paredes, 2010 [28]	- BWT - Vascularity pattern - Pathological parietal thickness - Positive CDS
Paredes, 2013 [29]	- BWT- Vascularity pattern on color Doppler - Pathological wall thickness
Ramaswamy, 2020 [30]	- BWT - Bowel wall stratification - Doppler activity within the bowel wall - Mesenteric fat (fatty wrapping) - Strictures - Fistulae - Abscess
Rispo, 2006 [31]	-BWT
Sagami, 2020 [33]	- BWT in the colon, terminal ileum, and rectum - CDS on segments with pathological wall thickness
Saevik, 2020 [34]	- BWT -CDS
Takahara, 2021 [35]	- BWT
Ripolles, 2021 [32]	- BWT - Wall vascularization CD - Wall echostructure - Mesenteric fatty proliferation - Images of wall ulcers - Complications (stenosis, fistulas, and abscesses) - Parameters obtained from contrast quantification
Yigit, 2022 [36]	BWT, mesenteric inflammation, lymphadenopathy, and complications

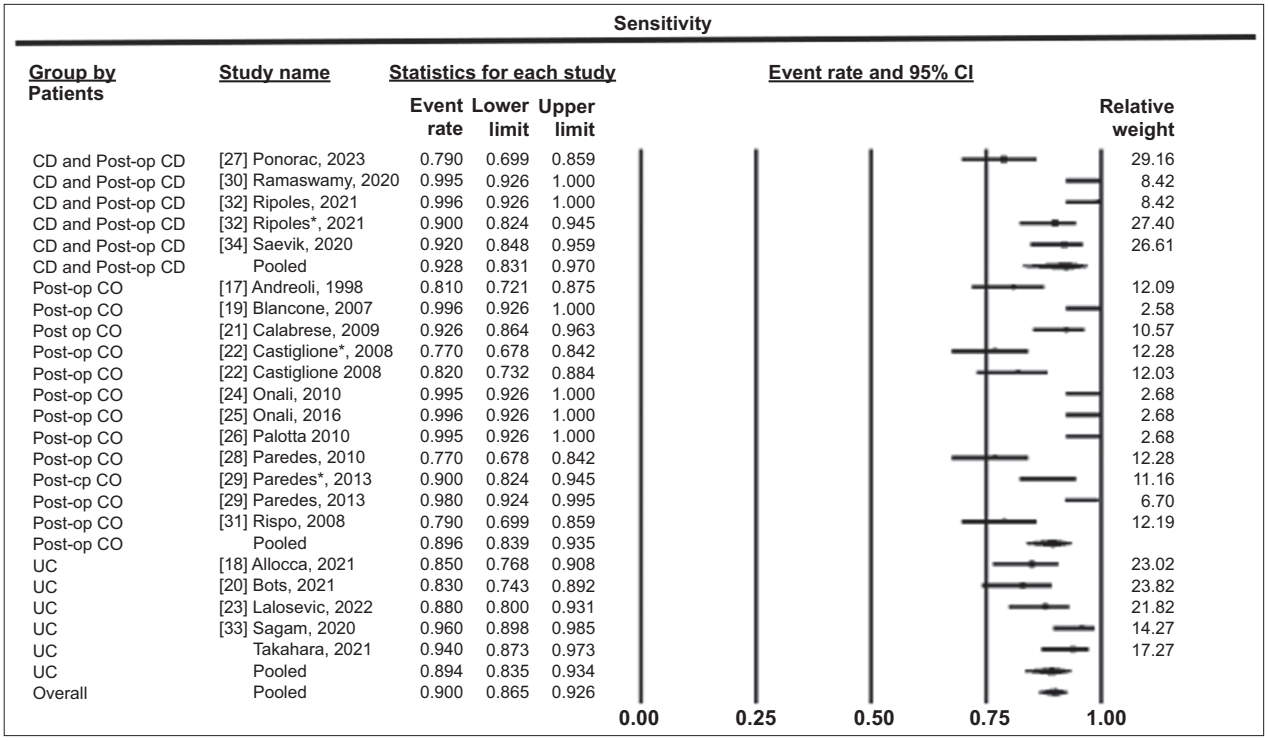
CWT, colonic wall thickening; CWP, colonic wall pattern; CWF, colonic wall pattern; BWT, bowel wall thickness; CDS, color Doppler signal; CD, Crohn's disease; CS, contrast sonograpghy; UCEIS, Ulcerative Colitis Endoscopic Index of Severity; PSR, postsurgical recurrence; SES-CD simplified endoscopic score for CD; MES, Mayo endoscopic subscore



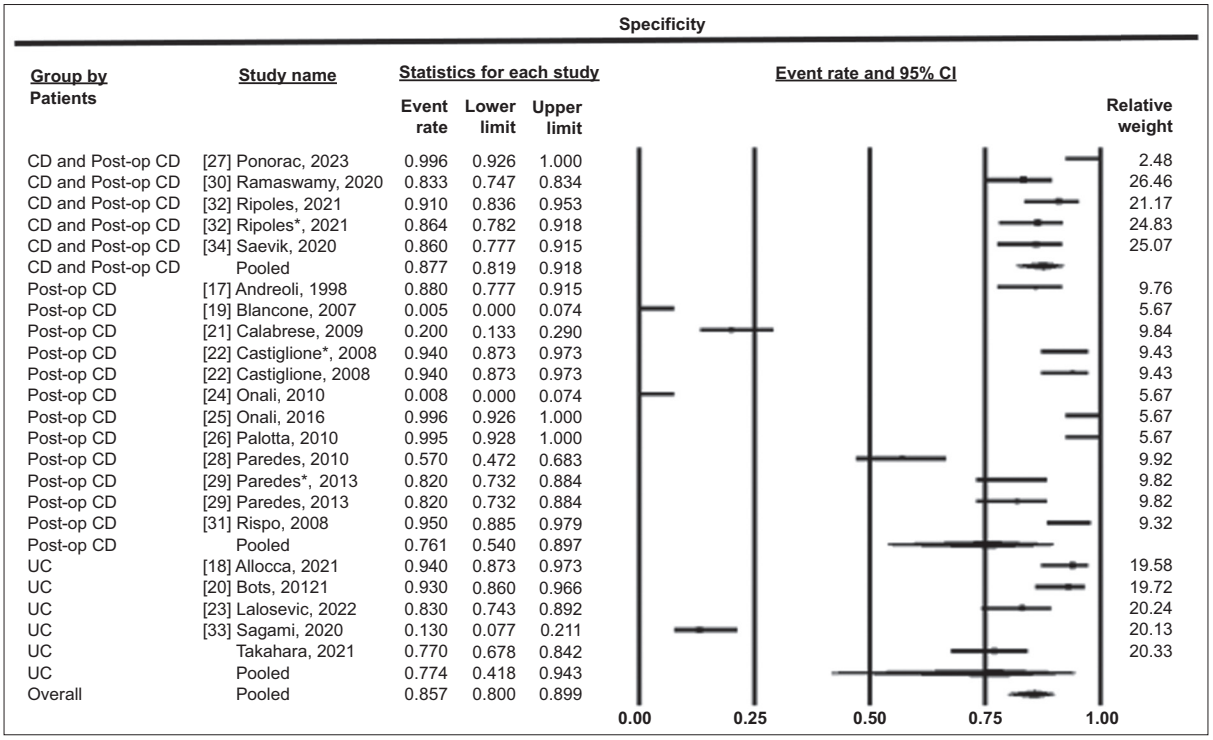
Supplementary Figure 1 Forest plot, PPV of BUS in IBD
PPV, positive predictive value; BUS, bowel ultrasound; IBD, inflammatory bowel disease; CI, confidence interval



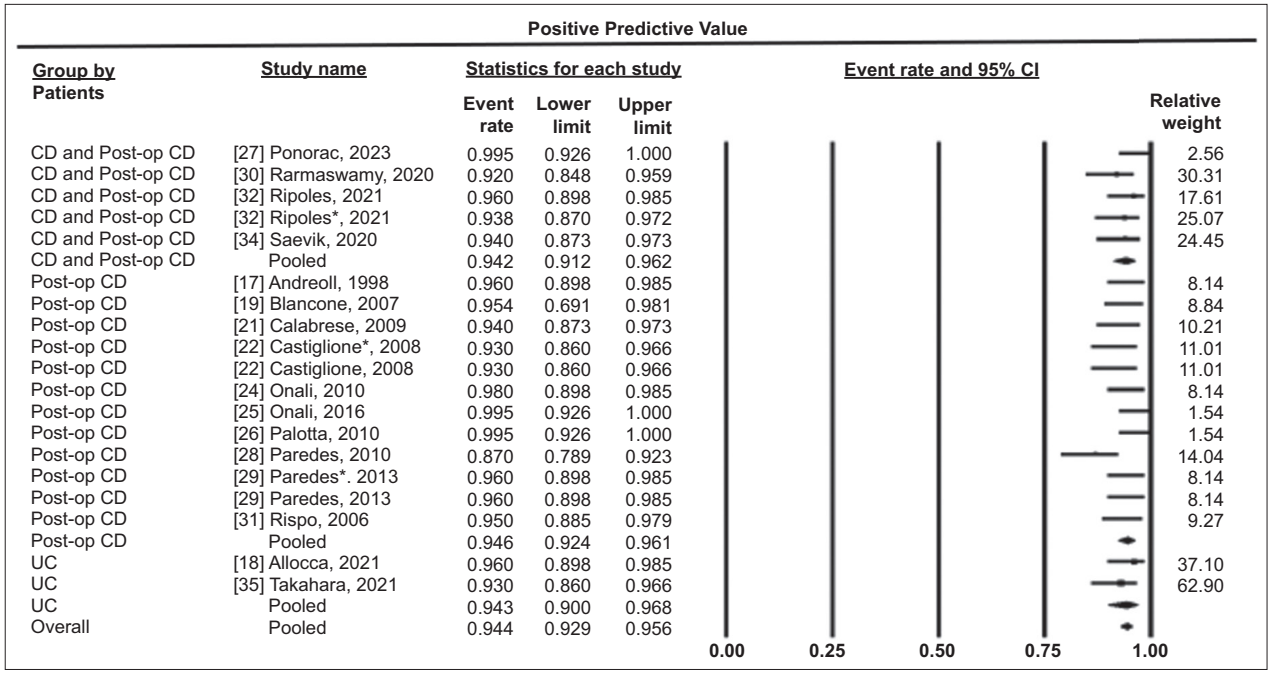
Supplementary Figure 2 Forest plot, NPV of BUS in IBD
NPV, negative predictive value; BUS, bowel ultrasound; IBD, inflammatory bowel disease; CI, confidence interval



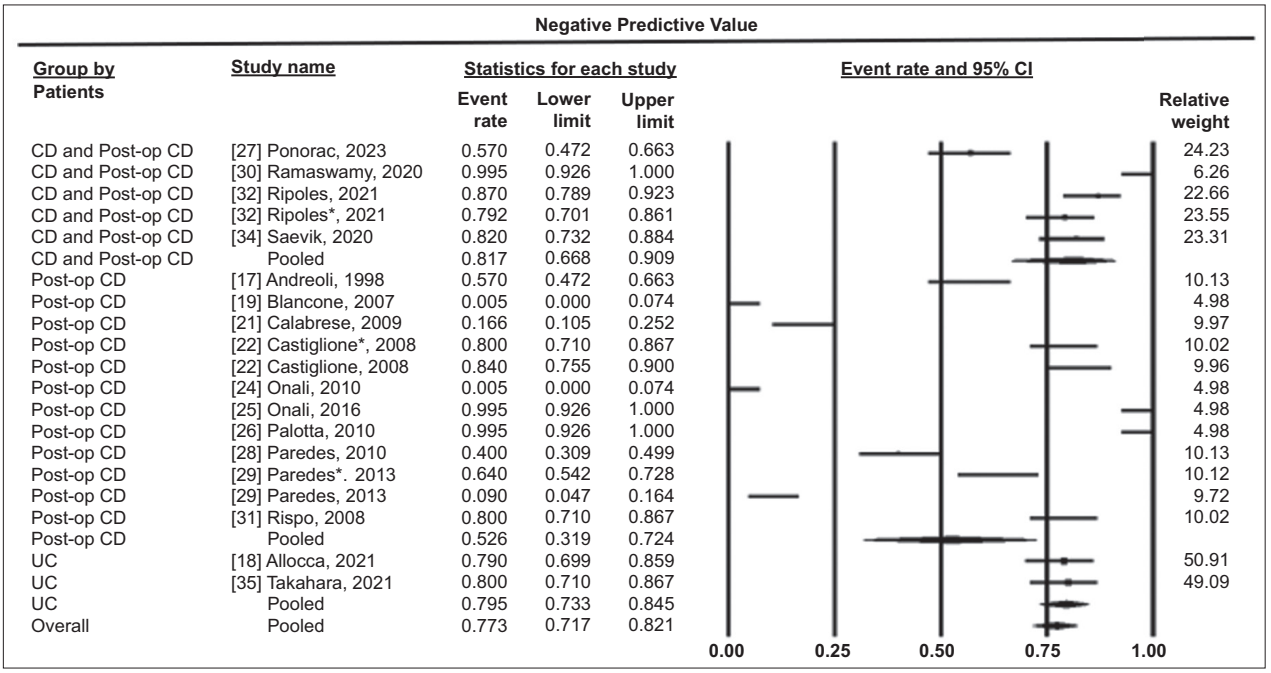
Supplementary Figure 3 Forest plot, sensitivity by type of inflammatory bowel disease
CD, Crohn's disease; UC, ulcerative colitis; CI, confidence interval



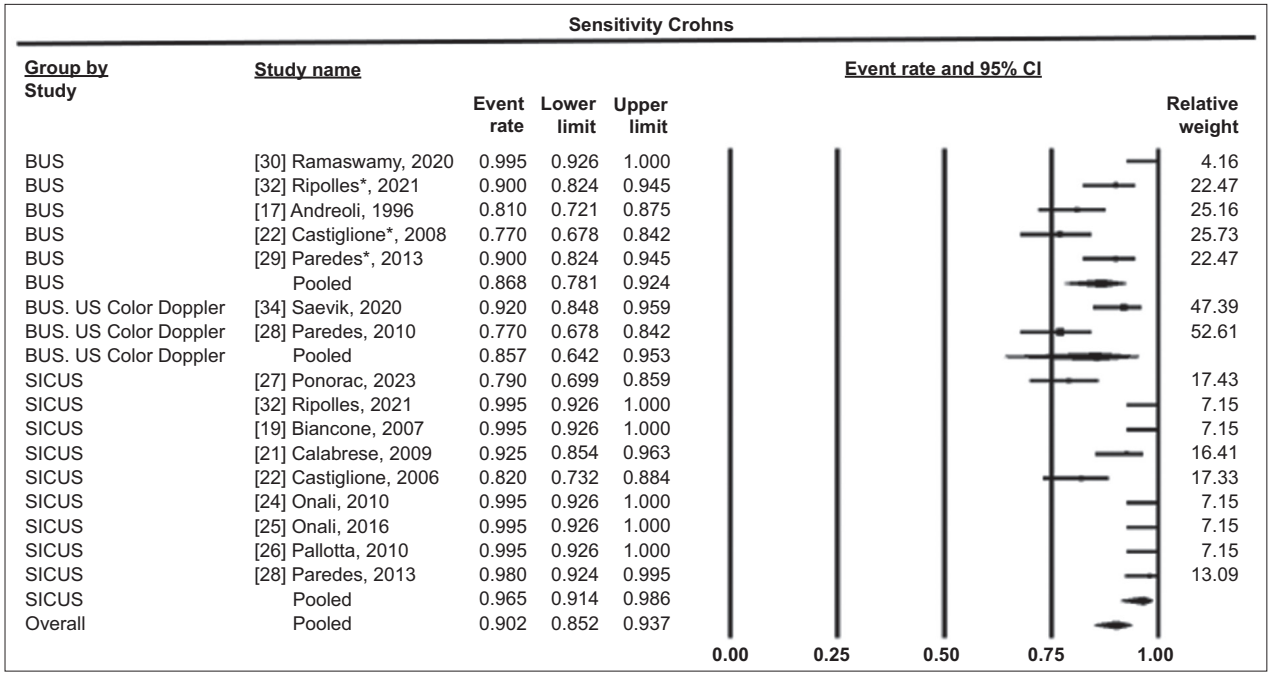
Supplementary Figure 4 Forest plot, specificity by type of inflammatory bowel disease
CD, Crohn's disease; UC, ulcerative colitis; CI, confidence interval



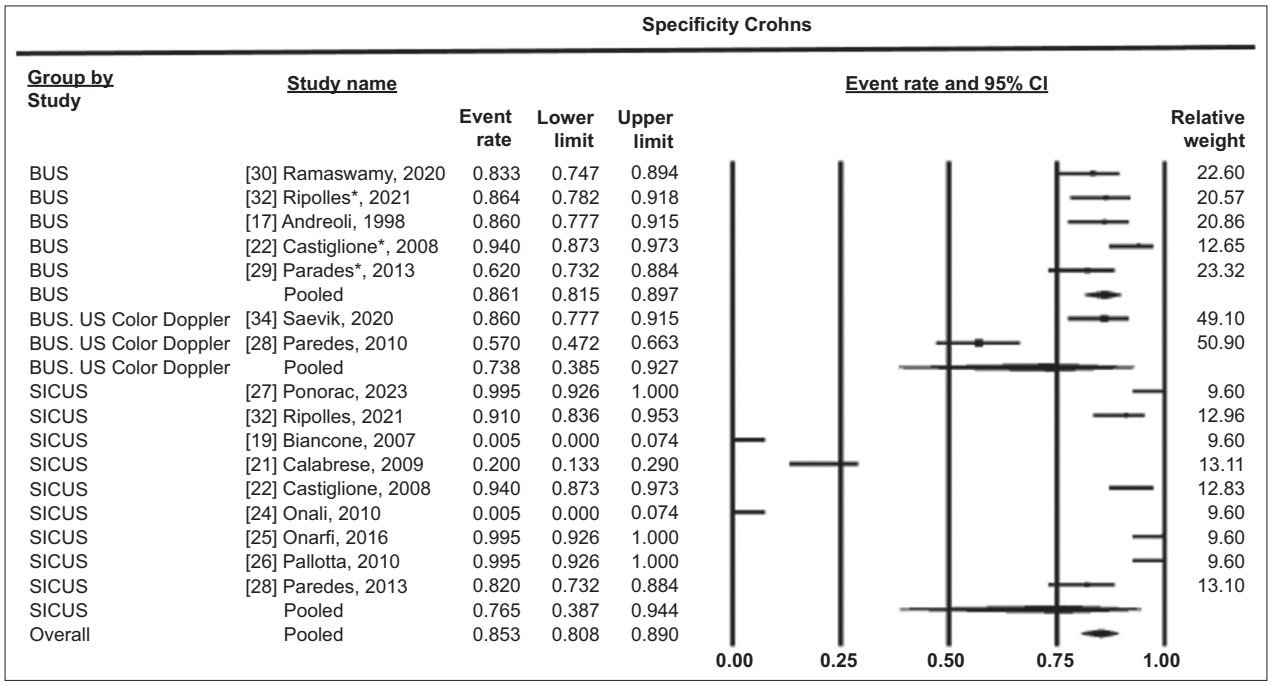
Supplementary Figure 5 Forest plot, positive predictive value by type of inflammatory bowel disease
CD, Crohn's disease; UC, ulcerative colitis; CI, confidence interval



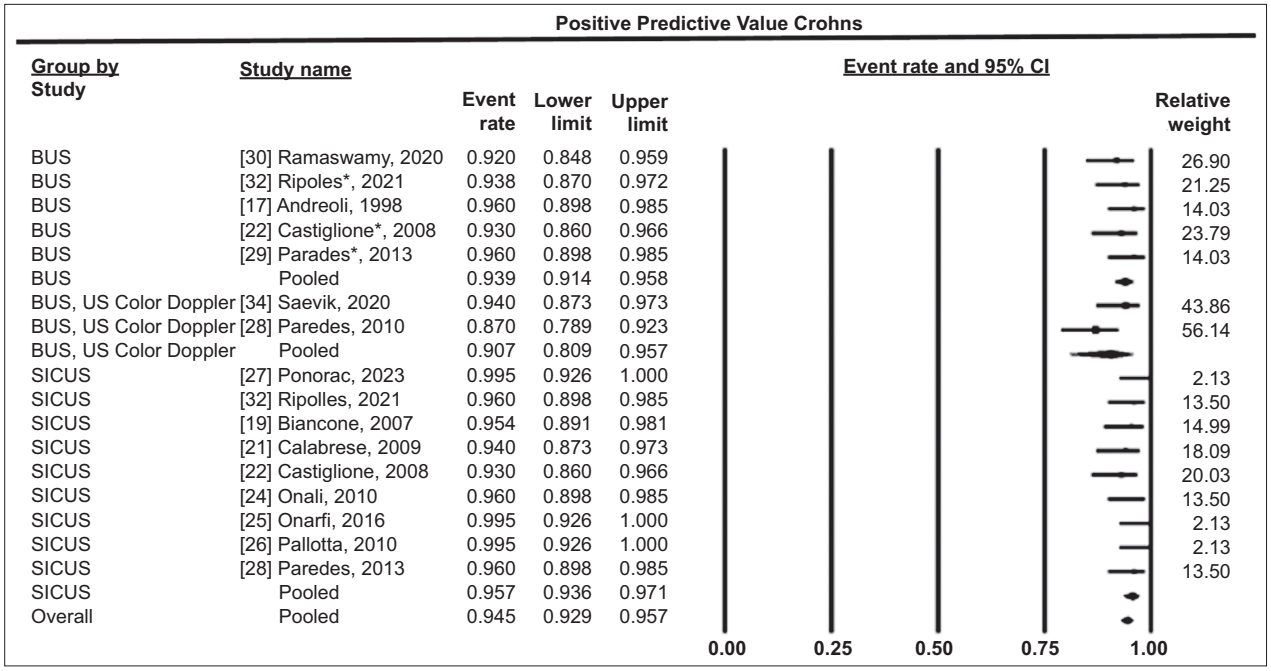
Supplementary Figure 6 Forest plot, negative predictive value by type of inflammatory bowel disease
CD, Crohn's disease; UC, ulcerative colitis; CI, confidence interval



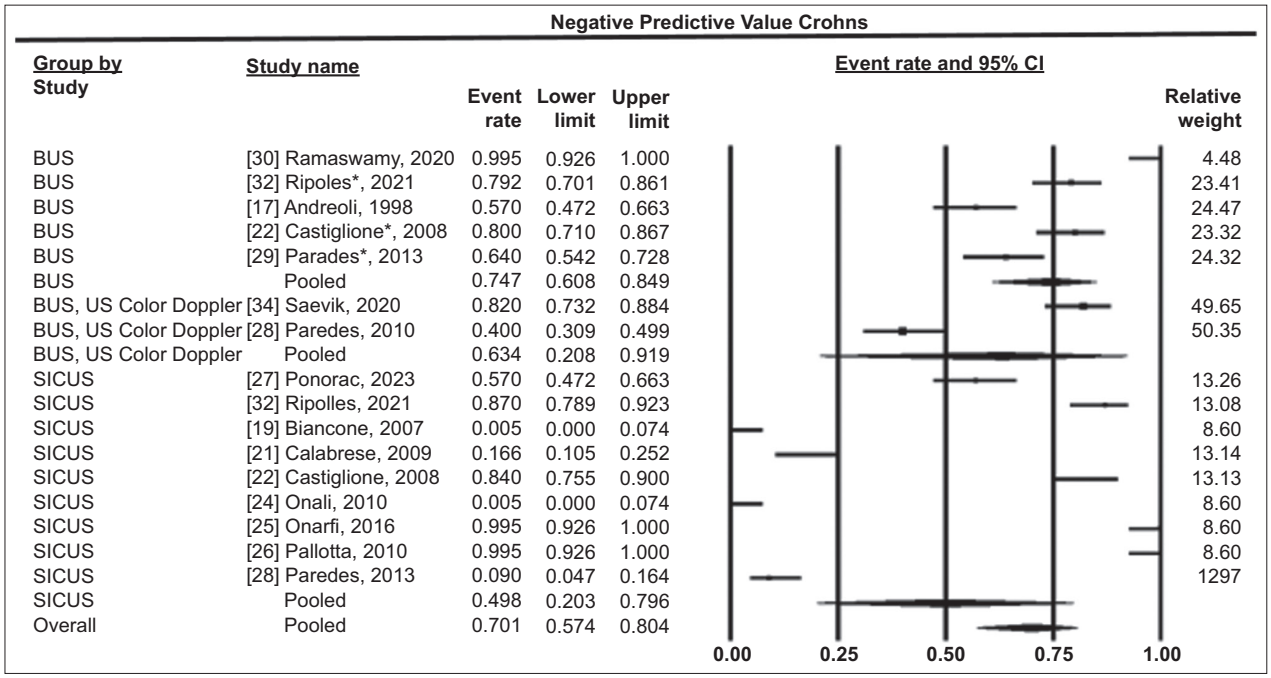
Supplementary Figure 7 Forest plot, sensitivity in CD and postoperative recurrence of CD by BUS subtypes
CD, Crohn's disease; BUS, bowel ultrasound; CUS, contrast ultrasonography; US, ultrasonography; BS, bowel sonography; CI, confidence interval



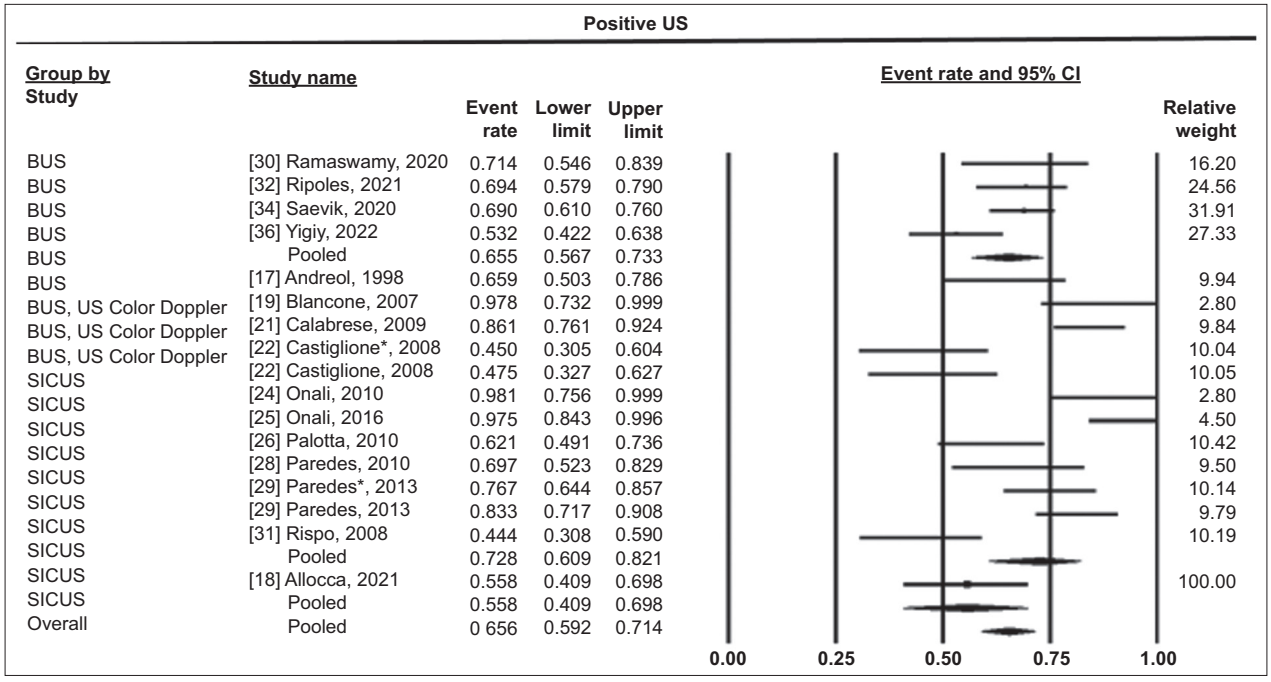
Supplementary Figure 8 Forest plot, specificity in CD and postoperative recurrence of CD by BUS subtypes
CD, Crohn's disease; BUS, bowel ultrasound; CUS, contrast ultrasonography; US, ultrasonography; BS, bowel sonography; CI, confidence interval



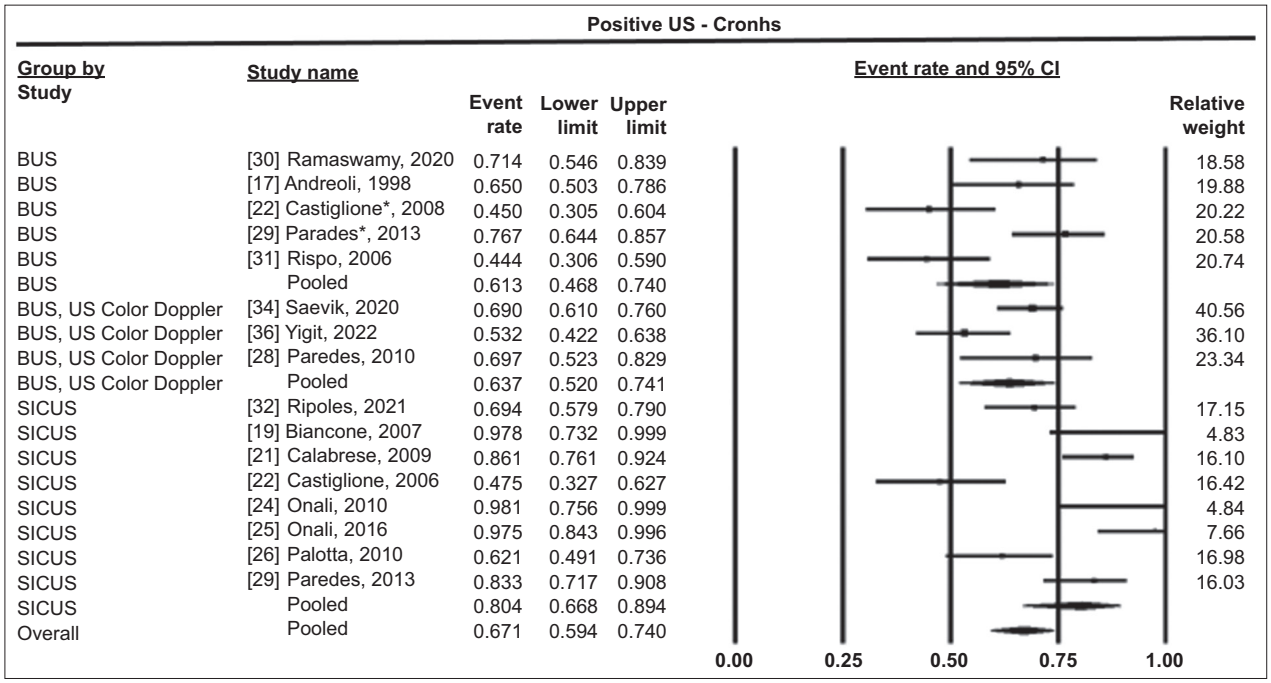
Supplementary Figure 9 Forest plot, PPV in CD and postoperative recurrence of CD by BUS subtypes
PPV, positive predictive value; CUS, contrast ultrasonography; US, ultrasonography; BS, bowel sonography; CI, confidence interval



Supplementary Figure 10 Forest plot, NPV in CD and postoperative recurrence of CD by BUS subtypes
NPV, negative predictive value; CUS, contrast ultrasonography; US, ultrasonography; BS, bowel sonography; CI, confidence interval



Supplementary Figure 11 Forest plot, positive ultrasound in IBD by BUS subtypes
IBD, inflammatory bowel disease; BUS, bowel ultrasound CD, Crohn's disease; UC, ulcerative colitis; CI, confidence interval



Supplementary Figure 12 Forest plot, positive ultrasound in CD and postoperative recurrence of CD by BUS subtypes
CD, Crohn's disease; BUS, bowel ultrasound; CUS, contrast ultrasonography; US, ultrasonography; BS, bowel sonography; CI, confidence interval

Appendices

Appendix 1 Literature search strategy

Searches ran on 05/06/2023

OVID

Database(s): Ovid MEDLINE(R) ALL (1946 to May 06, 2023), EBM Reviews - Cochrane Central Register of Controlled Trials May 2023, EBM Reviews - Cochrane Database of Systematic Reviews

#	Searches	Results
1	(Inflammatory Bowel Disease or Inflammatory Bowel Diseases or Ulcerative colitis or Crohn or Crohn's or IBD)	136275
2	(Ultrasonography or Ultrasonics or Ultrasound or sonograph* or ultrasonograph* or echo*)	853979
3	(Endoscopes, Gastrointestinal or Endoscopy, Gastrointestinal or Colonoscop*, or Ileocolonoscop*, or Endoscop*)	355247
4	1 and 2 and 3	975

PubMed, 3239 results (English only)

((ulcerative colitis [majr] AND ultrasonography [majr]) OR "ultrasound"[majr] OR "US"[majr] OR bowel ultrasound [tiab]) AND ("Crohn's disease"[majr] OR inflammatory bowel disease [tiab] OR IBD [tiab]) AND ("ultrasonography"[majr] OR "ultrasound"[majr] OR bowel ultrasound [tiab])

CINAHL

1	Endoscopes, Gastrointestinal OR Endoscopy, Gastrointestinal OR Colonoscop*, OR Ileocolonoscop*, OR Endoscop*	79,681
2	Ultrasonography OR Ultrasonics OR Ultrasound OR sonograph* OR ultrasonograph* OR echo*	209,743
3	Inflammatory Bowel Disease OR Inflammatory Bowel Diseases OR Ulcerative colitis OR Crohn OR Crohn's OR IBD	29,662
4	1 AND 2 AND 3	201

Cochrane

1	Endoscopes, Gastrointestinal OR Endoscopy, Gastrointestinal OR Colonoscop*, OR Ileocolonoscop*, OR Endoscop*	43,466
2	Ultrasonography OR Ultrasonics OR Ultrasound OR sonograph* OR ultrasonograph* OR echo*	79,407
3	Inflammatory Bowel Disease OR Inflammatory Bowel Diseases OR Ulcerative colitis OR Crohn OR Crohn's OR IBD	15,795
4	1 AND 2 AND 3	90

4505	total article references
1035	duplicates found in EndNote
3470	total references in EndNote

Appendix 2 PRISMA checklist

Section/topic	#	Checklist item	Reported on page #
		Title	
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
		Abstract	
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	5,6
		Introduction	
Rationale	3	Describe the rationale for the review in the context of what is already known.	7
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	7
		Methods	
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	7-9
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	7-9
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	7-9
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	7-9, Appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	7-9
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	7-9
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	7-9
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	8
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	7-9
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	7-9

(*Contd...*)

Appendix 2 (*Continued*)

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	8
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	9
		RESULTS	
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	9,10
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	9,10, Table 1, Table 2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	12, Supplementary Table 1
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	10-12, forest plot figures, Table 3
Synthesis of results	21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency	10-12
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	11
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	11,12
		DISCUSSION	
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12-14
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12-14
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	14
		FUNDING	
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	14

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