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Systematic Review

Terminal Ileum Intubation and Biopsy in Routine Colonoscopy Practice – A Systematic Review of Current Evidence

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Abstract

Background and objectives: Terminal ileum intubation is considered the completion step of colonoscopy and is usually performed to assess the ileum. The histological examination of the ileal mucosa, which is acquired during terminal ileum intubation, may allow an accurate diagnosis. However, there is no absolute consensus on when ileoscopy and biopsy should be attempted. As a result, we aimed to evaluate whether terminal ileum intubation and biopsy should be performed routinely.

Methods: Systematic searches were performed in the PubMed, EMBASE, and Cochrane Library databases, as well as the Science Citation Index via the Web of Science platform. Reference lists from the identified papers were manually searched. Systematic searches were performed from January 1, 1971, to October 1, 2025. Studies reporting on terminal ileum intubation and biopsy during colonoscopy were included. Case reports, letters, reviews, and animal studies were excluded. The primary outcomes were the diagnostic yield of terminal ileum intubation and the rate of necessitating a change in management. Data were extracted independently by three reviewers.

Results: Thirty-six studies were included. The subtotal diagnostic yield and the rate of necessary change among the selected patients were much greater than those among the unselected patients (5.1% versus 2.5% and 1.5% versus 0.4%, respectively). In addition, the diagnostic yield was found more frequently for inflammatory bowel disease, anemia, abdominal pain, and chronic diarrhea than for the other indications (26.7%, 16.1%, 14.9%, 12.4%, and 3.2%, respectively). The yield of ileal histopathology with a normal endoscopic appearance was low in both unselected and selected patients (3.5% and 2.4%, respectively).

Conclusions: Terminal ileum intubation is recommended as gold standard for completing colonoscopy. Biopsy should be considered in patients with abnormal endoscopic findings or specific high-risk symptoms.

Introduction

Since the first report of successful terminal ileum (TI) intubation by Nagasako in 1971,[1] there have been several reports describing the technical aspects, success rates, diagnostic yield, and biopsy outcomes in diseases involving the TI. TI intubation occurs during colonoscopy by many clinicians,[2–4] and it plays an important role in diagnosing diseases. The TI hosts many toxic substances and is lined by specialized lymphoid tissue of the immune system; thus, ileoscopy is usually performed to assess the state of the ileum or to diagnose or exclude diseases such as inflammatory bowel disease (IBD), infectious diseases, and parasitic diseases,[5–7] especially in the post-COVID-19 period, where the expanding gastrointestinal manifestations of COVID-19 infection are difficult to distinguish.[8–10] Furthermore, histological examination of the ileal mucosa acquired during TI intubation may facilitate accurate and

Keywords: Ileoscopy; Colonoscopy; Endoscopy; Intubation; Ileum; Biopsy; Inflammatory bowel disease; Diagnostic yield.

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definitive diagnoses, and some small bowel inflammatory diseases can only be diagnosed by ileoscopy.[11,12] All of these factors make TI intubation an appealing diagnostic technique during colonoscopy.

However, there is no absolute consensus on when ileoscopy should be attempted. Some physicians believe that this approach is an important adjunct to colonoscopy and should be used in all cases if the circumstances allow it.[13] This may necessitate a change in management. Others believe that this treatment option is optional, depending on the indications and after considering the discomfort, time, yield, special techniques, and unnecessary risks.[14,15] It also remains controversial whether an ileal biopsy should be attempted in patients undergoing TI intubation. As a result, evaluation and biopsy of the TI are left to the discretion of endoscopists according to their clinical experiences, after considering the indications, patient tolerance, operating techniques, and other difficulties during the examination.

This study was designed to ascertain whether TI intubation is a useful procedure for all patients who undergo a colonoscopy. We also aimed to further evaluate which clinical indication is more warranted with a higher diagnostic yield. Third, we evaluated whether TI biopsy should be performed in every patient despite a normal endoscopic appearance.

Materials and methods

A systematic search was performed in PubMed from January 1, 1971, to October 1, 2025, using the search terms "terminal ileums OR terminal ileum intubation OR ileum", "intubations OR intubating OR catheterization OR intubate OR intubated OR intubation", "ileoscopy OR ileoscopies OR ileocolonoscopy", "yield OR diagnosis OR diagnose OR diagnosed OR diagnoses", and "biopsies OR pathology OR biopsy". Reference lists from the identified papers were further hand-searched to identify relevant studies. The EMBASE, Cochrane Library, and Science Citation Index were also searched for these topics.

The searches were restricted to English-language results. Articles were selected if the abstract contained a yield or biopsy of the TI in the form of published trials, other controlled or comparative studies, or case series. Three reviewers (SW, ZH, and XH) independently retrieved the data. If there were any disagreements, the three reviewers referred to the relevant data, discussed the data, and finally reached a consensus. Some of these data were analyzed using chi-square analyses. This review was conducted in accordance with PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) 2020 guidelines. While not prospectively registered, we have documented the search strategy and inclusion criteria transparently.

Inclusion and exclusion criteria: The studies included in this systematic review were those performed on TI intubation during colonoscopy and were not randomized controlled trials. Case reports, letters, systematic reviews, and studies on animals or cell lines were excluded. When there were duplicate studies, the study with the largest sample size was included.

Qualitative analysis and data extraction

Two authors extracted the data separately, and the results were compared. If there was any disagreement, the authors discussed the study with a third author and reached a final conclusion. We used Review Manager 5.0.16 (Cochrane Collaboration, Oxford, UK) to summarize the details of the studies. The extracted data included the first author, publication year, country, inclusion criteria, age and sex of the patients, study design, indication for colonoscopy, and outcomes. The outcomes included the TI intubation rate, yield of TI intubation, yield of TI biopsy, diagnostic yield, and rate of necessitating a change in management.

The TI intubation rate was defined as the proportion of TI intubations relative to the total number of colonoscopies. The yield of TI intubation was defined as the ratio of the number of patients with abnormal TI findings after TI intubation to the total number of TI intubations. The yield of TI biopsy was defined as the ratio of the number of patients with TI histopathological findings through TI biopsy to the total number of TI biopsies. The diagnostic yield was defined as the ratio of the number of patients with endoscopic or histopathological findings that led to clinical intervention through TI intubation to the total number of TI intubations. The rate of need for a change in management was defined as the ratio of the number of patients who received a new diagnosis or one we believed would lead to specific investigations or management, such as therapy initiation, further imaging, or surgical intervention, through TI intubation to the total number of TI intubations. Patients with diarrhea, abdominal pain, weight loss, high C-reactive protein level, and hypoalbuminemia, along with previous negative stool testing for infection, were defined as having a high pretest probability of Crohn's disease.[16] Significant ileum histology was defined as histopathological findings from biopsy specimens of endoscopically normal-appearing ileal mucosa that necessitate a clinical intervention.

It was inappropriate to perform a meta-analysis due to the significant clinical heterogeneity of the studies. Based on their design, the studies were categorized into randomized crossover trials, randomized parallel-group trials, and non-randomized controlled trials. In addition, the methods of TI intubation and main outcome assessments varied.

Statistical analysis

Descriptive statistics were used to summarize study characteristics. Categorical variables are presented as percentages, and continuous variables are presented as mean ± standard deviation or mean as appropriate. Categorical variables were evaluated with a chi-square test or Fisher's exact test. A P-value of <0.05 was considered to indicate statistical significance, and all tests were two-sided.

Patient and public involvement statement

Patients or the public were not involved in the design, conduct, reporting, or dissemination plans of our research.

Results

We included 975 studies, and the process of identifying relevant studies is shown in Figure 1. Of the 975 initially potentially relevant studies, 24 were duplicates, and 923 were case reports, letters, systematic reviews, or irrelevant studies. Thus, 28 studies were included, and eight were acquired by manually searching the reference lists. Finally, 36 studies were included.[3,5–7,14,17–47] Of these, 15 were prospective studies, and the remaining 21 were retrospective. We defined "selected research" as TI intubation performed to investigate the etiology of a certain group of patients with symptoms of underlying digestive diseases, while "unselected research" refers to TI intubation performed on all unscreened patients undergoing colonoscopy, without prior selection based on specific digestive symptoms under investigation.

The basic characteristics and diagnostic yield of the included

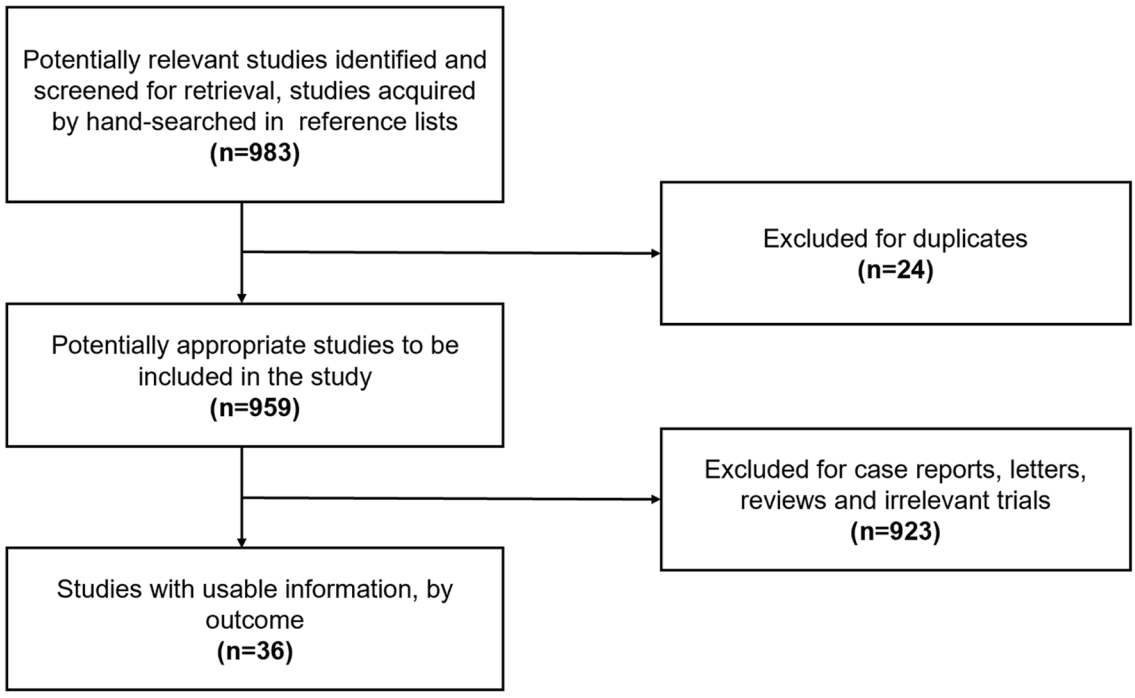

Fig. 1. Flow diagram of included and excluded studies.

studies are summarized in Table 1.[3,5–7,14,17–47] Eleven studies were from Europe, ten from the USA, eleven from Asia, two from Brazil, one from Australia, and one from Nigeria. The median number of TI-treated patients was 358. The success rate of TI intubation ranged from 30.9% to 100% among the prospective studies. The yield of TI intubation varied from 0.4% to 41%. The lowest incidence was reported in the study by Harewood *et al*.,[22] where only 17 abnormalities were found in 3,858 unselected patients who underwent TI assessment; the highest incidence was reported in the study by Geboes *et al*.,[5] where endoscopic lesions of the TI were found in 123 of 300 patients.

The yields of the TI biopsies were separated into three parts: biopsies obtained from endoscopically normal TIs, biopsies acquired from endoscopically abnormal TIs, and biopsies of unknown origin. Generally, routine biopsy of a normal macroscopic TI has a low diagnostic yield, ranging from 0% to 8.5%, while the yield of endoscopically abnormal TIs varies from 8.8% to 73.8%.

The diagnostic yield and rate of necessitating a change in management are summarized in Table 2.[3,5–7,14,17–28,30,32–46] A total of 33 studies reported the diagnostic yield of ileoscopy; 26 studies included patients who were unselected, and seven studies focused on patients with diarrhea. The diagnostic yield in all patients was 2.6% (995 abnormalities were found in 37,722 patients); 0.5% of patients changed their management. The percentage of patients with a total diagnostic yield was much greater among the selected patients than among the unselected patients (5.1% vs. 2.5%) (χ^2 = 61.01, $P < 0.0001$). The percentage of patients necessitating a change in management among the selected patients was twice as high as that among the unselected patients (1.5% vs. 0.4%) (χ^2 = 60.36, $P < 0.0001$).

The indications for colonoscopies in patients with successful TI intubation are documented in Table 3,[3,5,6,19,21,23,24,26,28,31,32,35,36,38,40,43] with a total of 24,077 patients in 16 studies, 22,698 unselected patients in 12 studies, and 1,379 selected patients in four studies. The most common indications for unselected patients were IBD, anemia, abdominal pain, and diarrhea. Compared with all other indications, diagnostic yield was more common for known IBD, anemia, abdominal pain, and chronic diarrhea. These values were 26.7%, 16.1%, 14.9%, and 12.4%, respectively.

Melton *et al*.[31] screened asymptomatic patients for cancer—the "Other" group had the greatest proportion of abnormal ileoscopy findings (63%), but this did not explain the specific screening outcomes to be excluded. Table 3 shows that the most common clinical indication was IBD (26.7%), which was more common during TI intubation. According to the four selected studies, patients with diarrhea had a diagnostic yield of 12.0%, which was similar to that of diarrhea patients in the previous 12 studies (χ^2 = 0.15, P = 0.69). However, the diagnostic value of the diarrhea group was significantly greater than that of the "Others" group for both the unselected and selected patients (χ^2 = 392.62, $P < 0.0001$; χ^2 = 10.41, $P < 0.01$).

It remains controversial whether biopsy via normal ileoscopy is suitable for clinical intervention, especially for patients with diarrhea. We assessed the yield of ileal histopathology with a normal endoscopic appearance, and the results are presented in Table 4.[3,5,18,19,21,25,26,29,32,34,35,45] Twelve studies were included; these consisted of seven studies involving unselected patients, and five studies involving patients with diarrhea. Of the 2,587 unselected patients who underwent ileoscopy, new information was added to 91 patients (3.5%) despite having normal endoscopic TI findings. In addition, histological assessment of biopsies from selected patients revealed abnormal findings in 22 of the 927 patients (2.4%), which was consistent with previous data from unselected patients (χ^2 = 2.87, P = 0.09).

Discussion

TI intubation is the gold standard for the completion of colonos-

Table 1. Basic characteristics of included studies in systematic review

Study (year)	Country	Sex (women, men)	Average years	Study design	Case selection	Patients (n)	Patients of TI intubation (n)	TI intubation rate
Borsch *et al*., 1984[17]	Germany		53.9	Prospective	Unselected	555	400	72.0%
Kundrotas *et al*., 1994[14]	USA	106, 164	Women 59, Men 61	Prospective	Unselected	270	213	78.9%
Zwas *et al*., 1995[6]	UK	–	–	Prospective	Unselected	144	138	95.8%
Geboes *et al*., 1998[5]	Belgium	Diarrhea (119, 138) Control (21, 22)	Diarrhea 35.8 (11–71) Control 47.6 (39–75)	Prospective	Diarrhea versus polyp surveillance (control)	300	Diarrhea 257, Control 43	100.0%
Bhasin *et al*., 2000[7]	India	–	–	Prospective	Unselected	66	57	86.4%
Shah *et al*., 2001[18]	USA	114, 54	51	Retrospective	Diarrhea	168	142	–
Yusoff IF, 2002[19]	Australia	621, 509	45	Retrospective	Diarrhea	1,131	508	–
Ansari *et al*., 2003[20]	UK	–	–	Prospective	Unselected	120	117	97.5%
Morini *et al*., 2003[21]	Italy	CNBD (56, 82) Control (56, 82)	–	Prospective	CNBD versus control	CNBD 156, Control 138	CNBD 138, Control 138	93.9%
Cherian *et al*., 2004[3]	UK	971, 733	60	Retrospective	Unselected	2,537	IBD 120, without IBD 1,584	–
Harewood *et al*., 2005[22]	USA	2,401, 1,457	–	Retrospective	Unselected	21,638	3,858	–
Yoong *et al*., 2006[23]	UK	–	–	Retrospective	Unselected	346	346	–
Iacopini *et al*., 2006[24]	Italy	336, 264	65	Prospective	Unselected	600	272	–
Powell *et al*., 2007[25]	UK	131, 101	52	Prospective	Unselected	232	232	–
McHugh *et al*., 2007[26]	USA	249, 165	37.6	Retrospective	Unselected	414	414	–
Kennedy *et al*., 2008[27]	USA	2,812, 3,596	63	Retrospective	Unselected	6,408	6,408	–
Jeong *et al*., 2008[28]	South Korea	1,782, 2,139	45	Prospective	Unselected	3,921	3,417	87.1%
Melo *et al*., 2009[29]	Brazil	47, 64	51.6	Prospective	Macroscopically normal terminal ileum mucosa	111	111	–
Emami *et al*., 2009[30]	Iran	73, 55	63	Prospective	Unselected	128	93	72.7%
Melton *et al*., 2011[31]	USA	6,009, 3,776	46	Retrospective	Unselected	9,785	9,785	–
Sayilir *et al*., 2011[32]	Turkey	–	–	Retrospective	CNBD versus others	295	CNBD 135, others 160	–
Makkar *et al*., 2013[33]	USA	464, 225	48.3	Retrospective	CNBD	689	370	–
Wijewantha *et al*., 2014[34]	Sri Lanka	–	–	Retrospective	Unselected	764	764	–
Koksal *et al*., 2014[35]	Turkey	142, 155	42	Retrospective	Normal-appearing TI and with <5 aphthous ulcers	297	297	–
Velidedeoğlu *et al*., 2015[36]	Turkey	24, 33	44.12 ± 11.42	Retrospective	Unselected	57	57	–
Akere *et al*., 2017[37]	Nigeria	–	–	Prospective	Unselected	272	84	30.9%
Meral *et al*., 2018[38]	Turkey	726, 584	55.79 ± 14.29	Prospective	Unselected	1,310	1,032	78.8%

(continued)

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Table 1. *(continued)*

Study (year)	Country	Sex (women, men)	Average years	Study design	Case selection	Patients (n)	Patients of TI intubation (n)	TI intubation rate
Borsotti *et al*., 2019[39]	Italy	–	–	Prospective	CNBD	504	492	97.6%
Mari *et al*., 2020[40]	Israel	878, 922	–	Retrospective	Unselected	1,800	1,800	–
Leiman *et al*., 2020[41]	USA	4,411, 3,388	58 (52–64)	Retrospective	Unselected	7,799	3,356	–
Wang *et al*., 2020[42]	China	774, 901	49	Retrospective	Unselected	1,675	994	–
Rosevics *et al*., 2021[43]	Brazil	2,181, 1,201	56.9 ± 13.1	Retrospective	Unselected	3,382	3,382	–
Alkhatib *et al*., 2022[44]	USA	461, 547	51.7	Retrospective	Unselected	1,008	1,008	–
Vora *et al*., 2024[45]	USA	185, 114	52	Retrospective	Macroscopically normal terminal ileum mucosa	299	299	–
Shu *et al*., 2024[46]	China	4,004, 3,595	53	Retrospective	Unselected	7,599	7,599	–
Dąbkowski *et al*., 2025[47]	Poland	169, 128	55.2	Retrospective	Unselected	297	297	–
TOTAL	–	–	–	–	–	7,884	6,619	84.0% (6,619/7,884)

Study (year)	Yield of TI intubation (%)	Yield of TI biopsy, by indication where available (%)		All cases (%)	Diagnostic yield†	Rate of necessitating a change in management‡	§Note
		Endoscopically normal TI (%)	Endoscopically abnormal TI (%)				
Borsch *et al*., 1984[17]	–	–	–	5.0%	5.0%	–	1
Kundrotas *et al*., 1994[14]	2.0%	Not biopsy	25.0%	–	0.5%	0.5%	2
Zwas *et al*., 1995[6]	–	–	–	Asymptomatic 2.7%, Diarrhea 29%	Overall 7.2%, Asymptomatic 2.7%, Diarrhea 29%	2.9%	3
Geboes *et al*., 1998[5]	Overall 41%, Diarrhea/ CD 47.8%, Control 0%	1.10%	–	Diarrhea/ CD 48.6%, Control 0	–	–	3
Bhasin *et al*., 2000[7]	22.8%	–	–	–	22.8%	8.8%	1
Shah *et al*., 2001[18]	–	2.4%	–	–	3.5%	1.4%	2
Yusoff *et al*., 2002[19]	5.1%	0	–	–	5.1%	2.6%	1
Ansari *et al*., 2003[20]	17.9%	–	–	2.6%	20.5%	–	3
Morini *et al*., 2003[21]	CNBD 34.0%, Control 10.8%	CNBD 2.2 % Control 2.4%	CNBD 46.8% Control 13.3 %	–	CNBD 17.4%, Control 3.6%	–	2
Cherian *et al*., 2004[3]	IBD 16.7%, without IBD 2.59%	Overall 1.5%, IBD 0, without IBD 1.7%	–	IBD 19%, without IBD 7.4%	4.1%	–	2
Harewood *et al*., 2005[22]	0.4%	–	–	–	0.4%	–	1
Yoong *et al*., 2006[23]	Abdominal mass 33.3%, Diarrhea 9.2^	–	–	4.6%	4.6%	2.3%	2
Iacopini G, 2006[24]	5.5%	–	–	2.2%	2.2%	2.2%	2
Powell *et al*., 2007[25]	–	2.3%	–	–	2.2%	0.0%	2

(continued)

Table 1. *(continued)*

Study (year)	Yield of TI intubation (%)	Yield of TI biopsy, by indication where available (%)		All cases (%)	Diagnostic yield†	Rate of necessitating a change in management‡	§Note
		Endoscopically normal TI (%)	Endoscopically abnormal TI (%)				
McHugh *et al*., 2007[26]	19.3%	5.1%, significant histologic chronic inflammation 4.2%	73.8%, significant histologic chronic inflammation 67.5%	18.4%	18.4%	–	2
Kennedy *et al*., 2008[27]	1.0%	Not biopsy	32%	0.3%	0.3%	0.04%	2
Jeong *et al*., 2008[28]	Overall 3.7%	Not biopsy	Overall 8.8%, Right lower quadrant pain 1.8%, Diarrhea 0.4	–	0.3%	0.1%	2
Melo *et al*., 2009[29]	–	0.9%	–	–	–	–	2
Emami *et al*., 2009[30]	4.3%	–	–	–	4.3%	2.2%	1
Melton *et al*., 2011[31]	Overall 24.9%	Total 5.0%, CD 10.9%	Total 47.7%, CD 75.0%	–	–	–	–
Sayilir *et al*., 2011[32]	–	Overall 4.4 %, CNBD 5.9%, Other 3.1%	–	–	Overall 4.4 %, CNBD 5.9%, Other 3.1%	0.0%	2
Makkar *et al*., 2013[33]	–	–	–	5.1%	5.1%	1.6%	2
Wijewantha *et al*., 2014[34]	7.1%	3.8%	37.0%	6.2%	10.6%	6.2%	2
Koksal *et al*. 2014[35]	33.0%	8.5%	Overall 59.8%	25.3%	25.3%	–	2
Velidedeoğlu *et al*., 2015[36]	–	–	14%	14%	14%	1.8%	2
Akere *et al*., 2017[37]	2.4%	–	–	17.9%	17.9%	–	2
Meral *et al*., 2018[38]	Overall 6%, IBD 14.1% chronic diarrhea 12.1%	Not biopsy	62.9%	–	3.8%	–	2
Borsotti *et al*., 2019[39]	11.4%	–	–	10%	3%	3%	2
Mari *et al*., 2020[40]	12%	–	–	12%	12%	–	2
Leiman *et al*., 2020[41]	1.1%	–	50%	0.1%	0.1%	–	2
Wang *et al*., 2020[42]	–	–	–	0.8%	0.8%	–	2
Rosevics *et al*., 2021[43]	5.3%	–	50.84%	2.7%	2.7%	0.9%	2
Alkhatib *et al*., 2022[44]	3.7%	Not biopsy	48.6%	–	1.8%	1.8%	2
Vora *et al*., 2024[45]	–	4.3%	–	4.3%	1.3%	1.3%	2
Shu *et al*., 2024[46]	2%	–	–	2.0%	0.1%	0.1%	2
Dąbkowski *et al*., 2025[47]	1.7%	–	–	1.7%	–	–	1

†Diagnostic yield: The diagnostic yield, a poorly defined concept, is sometimes used as a surrogate for "endoscopic or histopathologic findings that lead to a clinical intervention". ‡Necessitate a change in management: It raised a new diagnosis or, if we believed it would lead to specific investigations or management. §Note: The "Diagnostic yield" and "Necessitate a change in management" result from macroscopic (1), microscopic (2), and unclear (3) abnormalities. CD, Crohn's disease; CNBD, chronic nonbloody diarrhea; IBD, inflammatory bowel disease; TI, terminal ileum.

Table 2. Diagnostic yield of terminal ileum intubation with or without biopsy

Study (year)	Patients of TI intubation (n)	Case selection	Diagnostic yield (%)	Necessitate a change in management (%)	Diagnostic yield (n)	Necessitate a change in management (n)	Note[†]
UNSELECTED							
Borsch *et al*., 1984[17]	400	Unselected	5.0%	–	20	–	1
Kundrotas *et al*., 1994[14]	213	Unselected	0.5%	0.5%	1	1	
Zwas *et al*., 1995[6]	138	Unselected	7.2%	2.9%	10	4	
Bhasin *et al*., 2000[7]	57	Unselected	22.8%	8.8%	13	5	
Ansari *et al*., 2003[20]	117	Unselected	20.5%	–	24	–	
Cherian *et al*., 2004[3]	1,704	Unselected	4.1%	–	70	–	
Harewood *et al*., 2005[22]	3,858	Unselected	0.4%	–	17	–	
Yoong *et al*., 2006[23]	346	Unselected	4.6%	2.3%	16	8	
Iacopini *et al*., 2006[24]	272	Unselected	2.2%	2.2%	6	6	
Powell *et al*., 2007[25]	232	Unselected	2.2%	0	5	0	
McHugh *et al*., 2007[26]	414	Unselected	18.4%	–	76	–	
Kennedy *et al*., 2008[27]	6,408	Unselected	0.3%	0.04%	22	3	
Jeong *et al*., 2008[28]	3,417	Unselected	0.3%	0.1%	11	3	
Emami *et al*., 2009[30]	93	Unselected	4.3%	2.2%	4	2	2
Wijewantha *et al*., 2014[34]	764	Unselected	10.6%	6.2%	81	47	
Koksal *et al*., 2014[35]	297	Normal-appearing TI and with <5 aphthous ulcers	25.3%	–	75	–	
Velidedeoğlu *et al*., 2015[36]	57	Unselected	14%	1.8%	8	1	
Akere *et al*., 2017[37]	84	Unselected	17.9%	–	15	–	
Meral *et al*., 2018[38]	1,032	Unselected	5.2%	–	54	–	
Mari *et al*., 2020[40]	1,800	Unselected	12%	–	216		
Leiman *et al*., 2020[41]	354	Unselected	0.6%	–	2		
Wang *et al*., 2020[42]	994	Unselected	0.8%	–	8	–	
Rosevics *et al*., 2021[43]	3,382	Unselected	2.7%	0.9%	90	30	
Alkhatib *et al*., 2022[44]	1,008	Unselected	1.8%	1.8%	18	18	
Vora *et al*., 2024[45]	299	Macroscopically normal terminal ileum mucosa	1.3%	1.3%	4	4	
Shu *et al*., 2024[46]	7,599	Unselected	0.1%	0.1%	7	7	
SUBTOTAL	35,339	–	2.5% (873/35,339)	0.4% (139/35,339)	873	139	
SELECTED							
Geboes *et al*., 1998[5]	300	Diarrhea/ CD versus polyp surveillance	5.0%	–	15	0	
Shah *et al*., 2001[18]	142	Diarrhea	3.5%	1.4%	5	2	
Yusoff *et al*., 2002[19]	508	Diarrhea	5.1%	2.6%	26	13	

(continued)

Table 2. *(continued)*

Study (year)	Patients of TI intubation (n)	Case selection	Diagnostic yield (%)	Necessitate a change in management (%)	Diagnostic yield (n)	Necessitate a change in management (n)	Note†
Morini *et al*., 2003[21]	276	CNBD versus control	CNBD 17.4%, Control 3.6%	–	24, 5	–	
Sayilir *et al*., 2011[32]	295	CNBD versus others	Overall 4.4 %, CNBD 5.9%, Other 3.1%	0.0%	Overall 13, CNBD 8, others 5	0	
Makkar *et al*., 2013[33]	370	CNBD	5.1%	1.6%	19	6	
Borsotti *et al*., 2019[39]	492	CNBD	3.0%	3.0%	15	15	
SUBTOTAL	2,383	–	5.1% (122/2,383)	1.5% (36/2,383)	122	36	
TOTAL	37,722	–	2.6% (995/37,722)	0.5% (175/37,722)	995	175	

†1:24.5% (98 patients) with normal investigation were of considerable clinical interest; 2: Normal ileum findings were also helpful in ruling out TI pathology in 78 other patients. CD, Crohn's disease; CNBD, chronic nonbloody diarrhea; TI, terminal ileum.

Table 3. Clinical indications for colonoscopy

Study (year)	Diarrhea		Abdominal pain		IBD		Anemia		Others		Note†
	n	Diagnostic yield	n	Diagnostic yield	n	Diagnostic yield	n	Diagnostic yield	n	Diagnostic yield	
UNSELECTED											
Zwas *et al*., 1995[6]	28	8 (28.6%)	7	0	–	–	7	0	96	2 (2.1%)	1
Cherian *et al*., 2004[3]	–	–	–	–	120	20 (16.7%)	–	–	1,584	41 (2.6%)	1
Yoong *et al*., 2006[23]	119	11 (9.2%)	74	2 (2.7%)	33	5 (15.2%)	36	4 (11.1%)	65	6 (9.2%)	1
Iacopini *et al*., 2006[24]	–	–	31	0.0%	–	–	45	2 (4.4%)	196	4 (2.0%)	2
McHugh *et al*., 2007[26]	135	14 (10.4%)	23	1 (4.3%)	157	45 (28.7%)	62	9 (14.5%)	37	7 (18.9%)	2
Jeong *et al*., 2008[28]	1,058	58 (5.5%)	1,254	48 (3.8%)	–	–	82	2 (2.4%)	1,522	17 (1.1%)	1
Melton *et al*., 2011[31]	5,108	735 (14.4%)	3,629	758 (20.9%)	1,644	460 (27.9%)	502	156 (31.1%)	–	–	1
Koksal *et al*., 2014[35]	–	–	–	–	23	8 (34.8%)	44	17 (38.6%)	–	–	2
Velidedeoğlu *et al*.,2015[36]	19	6 (31.6%)	14	0.0%	–	–	–	–	24	2 (8.3%)	
Meral *et al*., 2018[38]	74	9 (12.2%)	89	4 (4.5%)	85	12 (14.1%)	252	8 (3.2%)	532	29 (5.5%)	1
Mari *et al*., 2020[40]	–	–	–	–	72	32 (44.4%)	161	25 (15.5%)	–	–	
Rosevics *et al*., 2021[43]	421	27 (6.4%)	486	21 (4.3%)	273	61 (22.3%)	278	13 (4.7%)	2,197	85 (3.9%)	
SUBTOTAL	6,962	868 (12.5%)	5,607	834 (14.9%)	2,407	643 (26.7%)	1,469	236 (16.1%)	6,253	193 (3.1%)	
Range	–	5.5–31.6%	–	0.0–20.9%	–	14.1–44.4%	–	3.2–38.6%	–	1.1–18.9%	
SELECTED											

(continued)

Table 3. *(continued)*

Study (year)	Diarrhea		Abdominal pain		IBD		Anemia		Others		Note[†]
	n	Diagnostic yield	n	Diagnos-tic yield	n	Diagnostic yield	n	Diagnostic yield	n	Diagnostic yield	
Geboes *et al*., 1998[5]	257	44 (17.1%)	–	–	–	–	–	–	43	0 (0.0%)	1
Yusoff *et al*., 2002[19]	508	26 (5.1%)	–	–	–	–	–	–	–	–	1
Morini *et al*., 2003[21]	138	47 (34.1%)	–	–	–	–	–	–	138	15 (10.9%)	1
Sayilir *et al*., 2011[32]	135	8 (5.9%)	–	–	–	–	–	–	160	5 (3.1%)	2
SUBTOTAL	1,038	125 (12.0%)	–	–	–	–	–	–	341	20 (5.9%)	
Range	–	5.1–17.1%	–	–	–	–	–	–	–	0.0–10.9%	
TOTAL	8,000	993 (12.4%)	5,607	834 (14.9%)	2,407	643 (26.7%)	1,469	236 (16.1%)	6,594	213 (3.2%)	

[†]The "Diagnostic yield" results from macroscopic (1), microscopic (2), and unclear (3) abnormalities. IBD, inflammatory bowel disease.

Table 4. Yield of ileum histopathology with normal endoscopic appearance

Study (year)	Patients of TI intubation (n)	Case selection	Endoscopically normal (n)	Histopathology with normal ileum (n)	Significant ileum histology (%)
UNSELECTED[†]					
Cherian *et al*., 2004[3]	IBD 120, without IBD 1,584	Unselected	Overall 717, IBD 85, without IBD 632	Overall 11, IBD 0, without IBD 11	Overall 1.5%, IBD 0, without IBD 1.7%
Powell *et al*., 2007[25]	232	Unselected	216	5	2.3%
McHugh *et al*., 2007[26]	414	Unselected	334	17	5.1%
Melo *et al*., 2009[29]	111	Macroscopically normal terminal ileum mucosa	111	1	0.9%
Wijewantha *et al*., 2014[34]	764	Unselected	710	27	3.8%
Koksal *et al*., 2014[35]	297	Normal-appearing TI and with <5 aphthous ulcers	200	17	8.5%
Vora *et al*., 2024[45]	299	Macroscopically normal terminal ileum mucosa	299	13	4.3%
SUBTOTAL	3,821	–	2,587	91	3.5% (91/2,587)
SELECTED[†]					
Geboes *et al*., 1998[5]	300 (Diarrhea/ CD 257, Control 43)	Diarrhea /CD versus polyp surveillance (control)	177	2	1.1%
Shah *et al*., 2001[18]	142	Diarrhea	83	2	2.4%
Yusoff *et al*., 2002[19]	508	Diarrhea	158	0	0.0%
Morini *et al*., 2003[21]	CNBD138, Control138	CNBD versus control	214	5	2.3%
Sayilir *et al*., 2011[32]	295 (CNBD135, others160)	CNBD versus others	295	13	4.4%
SUBTOTAL	1,521	–	927	22	2.4% (22/927)
TOTAL	5,342	–	3,514	113	3.2% (113/3,514)

[†]In this table, "UNSELECTED" refers to an endoscopically normal appearance with no secondary screening based on specific symptoms within this subgroup. "SELECTED" refers to an endoscopically normal appearance with secondary screening based on specific symptoms. CD, Crohn's disease; CNBD, chronic nonbloody diarrhea; IBD, inflammatory bowel disease; TI, terminal ileum.

copy and is vital to the diagnostic process. Usually, colonoscopy documentation includes endoscopic visualization, photography, video of cecal landmarks, and TI intubation.[44] Unfortunately, photographs of the cecum often fail to convincingly demonstrate classical cecal landmarks, and the use of video is inconvenient. This approach results in better assurance of completion during terminal ileoscopy.[48] In addition, several studies have shown that failure to detect tumors during screening colonoscopy might result from an incomplete procedure.[22,30] A recent study reported a case of a small bowel neuroendocrine tumor in the TI detected through colonoscopy with TI intubation during screening. Although the overall diagnostic yield for malignant tumors remains low, TI evaluation continues to be a valuable tool in cancer screening.[49] Additionally, some small bowel inflammatory diseases can be established only by ileoscopy, and such diseases include Crohn's disease, which preferentially affects the small intestine—especially the TI.[50,51] In conclusion, TI endoscopy and biopsy are generally considered the gold standards for the differential diagnosis of infectious, inflammatory, and noninflammatory disorders that mimic IBD according to symptomatic and endoscopic findings.[35]

There have been no randomized controlled trials focusing on the role of ileoscopy or biopsy, and the evidence in our report mainly consists of retrospective/prospective observational studies and a case-control series. Studies have reported that the success rate of TI intubation varies from 72% to 97% when attempted,[18,19] with patients treated for no more than 3–4 m on average.[14] The reasons for unsuccessful intubation include technical difficulties, discomfort, obstructive lesions, retained blood, poor bowel preparation,[28] redundancy of the colon,[14] TI stricture, and inability to identify ileal openings.[7] While there are few complications,[7] a 79-year-old man was reported with a colonic perforation of the sigmoid diverticulum.[35] This was not associated with the performance technique. These features make TI intubation an appealing and applicable diagnostic method for colonoscopy.

Although several studies have described the yield of ileoscopy, it is still unclear whether TI intubation should be performed routinely in all patients. Some researchers believe that TI intubation should be a standard practice.[30] In several studies, ileoscopic findings revealing normal TI mucosa may also help to diagnose, differentiate, and rule out some mimicking diseases. In these cases, a normal TI or biopsy specimen helps to avoid further diagnostic studies and aids in making wise decisions for the next step of management.[14,30,35] Therefore, although the number of positive findings in unselected patients was low, normal TI intubation was also very helpful in clinical intervention. However, other researchers have suggested that TI intubation should not be performed for every patient due to the low yield.[5,23] In our analysis, ileoscopy rarely revealed pathological findings in unselected patients, while TI intubation might offer much more diagnostic information among selected patients, especially those with diarrhea.[5,18,19,21,32,33]

TI intubation has a high diagnostic yield when applied to specific clinical conditions, such as chronic nonbloody diarrhea and IBD.[5,6,18,21,39] It also plays an important role in the diagnosis of colonic tuberculosis, intestinal stricture, ileitis, and lymphoma.[52] We recommend considering TI intubation even when the procedural indication is related to the "upper gastrointestinal" tract or presents with nonspecific symptoms. A representative case reported by Amadu *et al*.[53] well illustrates this point: a 53-year-old woman presented with epigastric pain and showed no improvement after a course of proton pump inhibitors. Subsequent upper gastrointestinal endoscopy revealed persistent duodenal lesions. Ileoscopy performed concurrently demonstrated aphthous ulcers in the TI, and magnetic resonance imaging further indicated mild inflammation in the same region, ultimately leading to a diagnosis of duodenal Crohn's disease.[53] This case highlights that TI examination can provide critical clinical and endoscopic evidence when proximal gastrointestinal findings remain inconclusive.

Our findings in Table 2 demonstrated that routine TI intubation seldom provided diagnostic information, while its additional time cost significantly increased the workload on a national scale, impacted histopathological services,[23] and exacerbated patient discomfort. However, against the backdrop of the rising global prevalence of IBD and the clinically non-negligible incidence of incidental ileitis—including aphthous ulcers, erosions, nonsteroidal anti-inflammatory drug-induced enteropathy, and early Crohn's disease—we must also recognize the practical importance of establishing terminal ileal intubation as a standard step in most colonoscopies. This is based on two key considerations: first, early Crohn's disease frequently localizes to the TI, and missed diagnosis may lead to delayed treatment and disease progression; second, attempting intubation only in cases with strong indications may hinder the maintenance and improvement of endoscopists' technical proficiency. Therefore, incorporating the terminal ileal intubation rate as a quality key performance indicator will not only enhance the detection of pathological findings but also serve as an essential measure to ensure the quality of endoscopic practice.

For patients undergoing TI intubation, routine mucosal biopsy when the endoscopic appearance is normal is controversial. Yusoff *et al*.[19] verified that microscopic findings from normal ileoscopy in patients with chronic diarrhea did not contribute to their diagnosis. Nonetheless, Sayilir showed no significant difference in the yield of TI biopsies between patients who presented with chronic nonbloody diarrhea and those with other indications.[32] This finding is similar to our data—the yield of TI biopsy in unselected patients was 3.5%, and the percentage ranged from 0.9% to 8.5% in patients with a normal ileoscopy. The selected patients complaining of diarrhea had a subtotal yield of ileal histopathology with a normal endoscopic appearance of 2.4% (ranging from 0% to 4.4%). The low yield suggested little value in undertaking a biopsy in macroscopically normal TIs. However, some experts believe that a normal-appearing ileal mucosa may sometimes reveal significant pathological findings. Misra *et al*.[54] reported the diagnostic role of TI biopsies in patients with suspected intestinal tuberculosis. There have been cases of cytomegalovirus colitis and microsporidiosis diagnosed by biopsy of normal-appearing TIs.[5,6,32,54] Harewood and McHugh maintained that biopsies from normal-appearing mucosa in patients suspected of having Crohn's disease may yield histological abnormalities due to TI 'skipping' or intramural disease.[22,26] The results of a study by Samuel *et al*.[55] found that 10 of 24 (41.7%) patients with clinically active Crohn's disease who were assessed endoscopically demonstrated microscopic evidence of chronic inflammation. This finding suggests that TI biopsies may be useful in patients with Crohn's disease with a high pretest probability. It can also be argued that a normal TI biopsy result is useful in some cases to avoid subsequent or repeat ileoscopies. In light of this, adopting a targeted biopsy strategy in clinical practice may be the preferable approach. This strategy emphasizes precise sampling of suspicious lesions, thereby maintaining diagnostic accuracy while avoiding extensive random biopsies, ultimately improving efficiency, shortening procedure time, and reducing patient risk.

Beyond its diagnostic role, ileoscopy plays a crucial role in the postoperative management of Crohn's disease. For patients who have undergone ileocecal resection, endoscopic monitoring of the TI within six to twelve months after surgery is an essential process

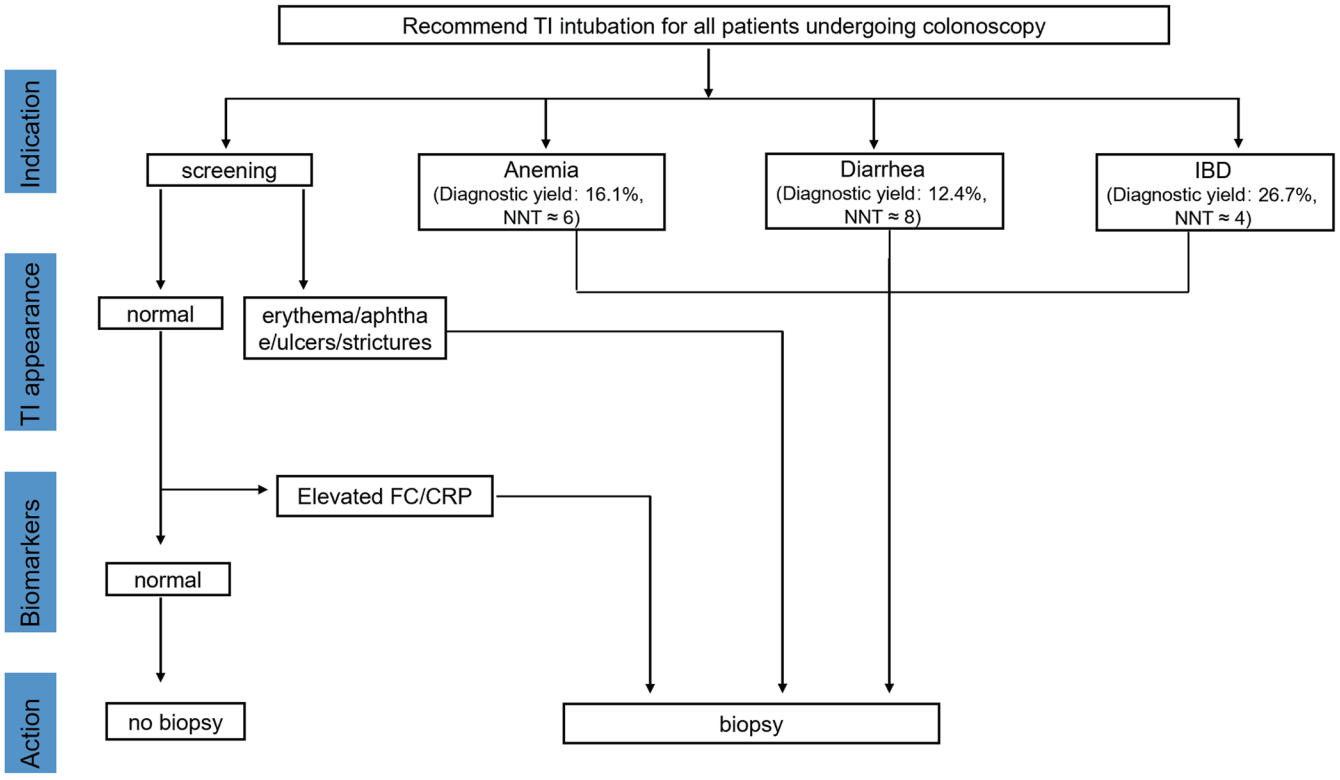

Fig. 2. Clinical decision algorithm for terminal ileal intubation and biopsy. CRP, C-reactive protein; FC, fecal calprotectin; IBD, inflammatory bowel disease; NNT, number needed to test; TI, terminal ileum.

for assessing and preventing recurrence.[56] The degree of endoscopic recurrence is standardized using the Rutgeerts score, which directly guides subsequent treatment strategies: a score ≥ i2 indicates moderate to severe recurrence, necessitating step-up intensification of therapy and timely adjustment or escalation of medication regimens to achieve endoscopic remission.[57] However, the timing of such monitoring endoscopy requires careful consideration. If patients experience postoperative infectious complications (such as surgical site infection, anastomotic leakage, or pneumonia) or have related high-risk factors (such as corticosteroid use, malnutrition, or perioperative blood transfusion),[58] endoscopic examination should be appropriately postponed until acute complications have fully resolved, nutritional status has improved, and immunosuppressive risks have been mitigated. The algorithm for deciding whether to obtain a terminal ileal biopsy is presented in Figure 2.

There are several limitations to our review. First, the included studies were predominantly observational in nature, exhibiting significant clinical and methodological heterogeneity. Second, the substantial heterogeneity observed among the included studies—such as the varying definitions of "diagnostic yield" and "need for a change in management" across different studies—precluded us from performing a formal meta-analysis or conducting a quantitative assessment of publication bias. Nevertheless, by providing weighted pooled estimates, number needed to test, and detailed outcome ranges, we have maximized the transparency and interpretability of the results. Third, our review was not prospectively registered (e.g., in PROSPERO), which may introduce reporting bias.

In summary, high-quality colonoscopy is essential for the screening and management of conditions such as colorectal tumors and inflammatory diseases, and terminal ileal intubation represents a key component of this procedure. To standardize this practice, it is recommended to document ileal landmarks—such as the ileocecal valve, plicae, and lymphoid follicles—with photographic records after intubation, while also monitoring and reporting TI intubation rates at the institutional level. Although the overall safety of colonoscopy is closely linked to sedation management, the risk of perforation during TI intubation itself is extremely low, particularly when performed by experienced operators. For beginners, mastering certain techniques can effectively shorten the learning curve. Methods such as applying retroflexion in the cecum, adhering to gentle suction and insufflation sequences, and utilizing the water exchange technique can significantly improve intubation success rates and enhance the patient experience.

Conclusions

Terminal ileal intubation is the gold standard for completing colonoscopy. It has a vital role in the diagnostic process. We recommend that TI intubation be adopted as standard practice and attempted in all patients with photo documentation. In cases with abnormal mucosal findings or red-flag symptoms—particularly diarrhea, suspected IBD, abdominal pain, or anemia—biopsy should be obtained.

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Conflict of interest

None.

Author contributions

Study conception and design (JQ, JG, XH, YB, ZL), acquisition of data (LG, TW), analysis and interpretation of data (JQ, JG, XH, LG, TW), drafting of the manuscript (JQ, JG), critical revision of the manuscript for important intellectual content (YS, ZH, YB, SW, ZL), study supervision (YB, ZL). All authors have made substantial contributions to this work and have approved the final manuscript.

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