The Yield of Ileoscopy: Does Indication Matter?

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ABSTRACT **Background:** While the routine performance of terminal ileum (TI) intubation during colonoscopy procedures is perceived to have a low yield, its utility during colonoscopies performed for specific indications have not been well studied.

Objectives: To assess the diagnostic yield of an indication-based ileoscopy in real-life practice.

Methods: The authors reviewed endoscopic reports of patients who underwent colonoscopies over an 8-year period (2011–2018) and had routine ileoscopy during these procedures. Demographic data, indications for colonoscopy, and endoscopic findings were documented. Diagnostic yield and odds ratio for TI findings were calculated.

Results: Over 30,000 colonoscopy reports performed during the study period were reviewed. Ilesocopy was performed in 1800 patients, 216 patients had findings in the TI (ileitis or ulcers). TI findings were more prevalent in younger ages (38.3 ± 17.6 vs. 43.6 ± 20, $P < 0.05$). The greatest yield of ileoscopy was evident when performed for the evaluation of chronic abdominal pain and diarrhea (14.4% vs. 9.3%, odds ratio [OR] 1.62, $P < 0.05$). Positive fecal occult blood test (FOBT) (OR 0.1, 95% confidence interval [95%CI] 0.02–0.5, $P = 0.005$) and constipation (OR 0.44, 95%CI 0.2–0.9, $P = 0.04$) were negatively associated with TI findings.

Conclusions: Ileoscopy may have the greatest utility in evaluating suspected inflammatory bowel disease (IBD) patients, but may not add value to the evaluation of constipation and positive FOBT.

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Colonoscopy is an endoscopic examination of the large bowel and occasionally the distal part of the small bowel. The examination can provide visual diagnosis and therapeutic interventions. Colonoscopy is considered the gold standard for colon cancer screening and surveillance [1,2]. Moreover, colonoscopy is used in the evaluation and diagnostic workup of numerous signs and symptoms related to a wide variety of gastrointestinal disorders and plays a crucial role in their diagnosis and management. In parallel, colonoscopy enables therapeutic interventions during the procedure including polypectomy, hemostasis, stricture dilation, stent placement, colonic decompression, and foreign body removal [3-5]. Performing a high-quality colonoscopy requires careful examination of the entire colonic mucosa. Quality indicators such as cecal intubation rates, withdrawal times, and adenoma detection rates has been developed and serve as surrogate markers for guiding consistent high-quality practice [6-9].

Although not considered as a quality metric, terminal ileum (TI) intubation can provide valuable diagnostic findings and may be used as a means of confirming colonoscopy completion when classical cecal landmarks are not confidently seen [10]. While several reports viewed TI intubation as a technically complicated and a time consuming skill that mandates higher sedation doses [11], other studies have shown that when the intubation of the TI was attempted routinely, visualization of the TI was achieved in as many as 95% of cases without complications [12]. Currently, no guidance is available regarding the suggested TI intubation rates. Ileal intubation has not been mandatory over the last decades, and ileoscopy is performed only during an average of 5–15% of the colonoscopies in the daily practice depending on the procedural indications, endoscopist preference and common practice [13]. Moreover, the diagnostic value of routine ileoscopy is not well documented and is widely debated. Commonly, TI intubation is performed mainly to diagnose or exclude inflammatory bowel disease (IBD). Variable diagnostic yields for TI intubation were reported when applied to specific clinical conditions, such as IBD [14], infectious ileitis [15], chronic diarrhea [16,17], lymphoma [18], and hematochezia [19]. In addition, the diagnostic yield of routine ileoscopy in different settings and indications in the daily common practice is still controversial. The aim of the current study was to assess the diagnostic yield of ileoscopy during colonoscopy exams according to procedural indications in real-life practice.

PATIENTS AND METHODS

We performed a single-center, retrospective study including all endoscopic reports of patients who had undergone colonoscopies during an 8-year period (2011–2018) within the gastroenterology department at the EMMS medical center in Nazareth, Israel. We

reviewed the electronic reports and included patients who had ileoscopy and full description of ileal findings during the colonoscopy procedure for the final analysis. In case of patients with repeated ileoscopies with similar results, we included the first procedure for final analysis. Patients with history of small bowel resection, those with poor bowel preparation, or when full dataset were missing, they were excluded from the study. The majority of the procedures were performed by four senior experienced endoscopists who performed these procedures or directly supervised their performance by trainees to ensure visualization and assessment of terminal ileum. Normal ileoscopy denoted findings of normal TI mucosa. Mild nodularity characteristic of lymphoid hyperplasia was also considered normal. Findings of erythema, friability, granularity, erosions, ulcers or strictures were considered as indicative of terminal ileitis.

Demographic data, indications for colonoscopy, and endoscopic findings of the TI were extracted and the diagnostic yield of ileoscopy according to procedure's indication was calculated using multiple logistic regression analysis to identify independent association between indication and TI findings. The study was approved by the local institution human research committee. Written informed consent was waived by the local ethics committee due to the retrospective non-interventional nature of the study.

STATISTICAL ANALYSIS

Characteristics of participants are presented with descriptive statistics as arithmetic means and standard deviation (SD) or range for continuous variables, or as frequencies (percentages) for categorical variables. The comparison of two independent groups was performed using Student's *t*-test for continuous variables and Chi-square statistic for continuous variables. Univariate regression analysis was used to estimate odds ratio (OR) of the endoscopic indications that were correlated with endoscopic findings. All tests applied were two-tailed. *P* value of 0.05 or lower was considered to be statistically significant. Statistical analyses were performed using SAS 9.4 software (SAS Institute Inc., Cary, NC, USA).

RESULTS

Overall, more than 30,000 colonoscopies were reviewed during the study period. The intubation of the TI was performed in 1800 patients and they were included for the final analysis. Among them, 216 patients had findings in the TI (ileitis or ulcers) (group A), while the remaining 1584 patients were considered to have a normal ileoscopy (group B). The average ages in group A and B were 38.3 ± 17.6 years and 43.6 ± 20 years, respectively. In group A, 123 patients (56.9%) were males as compared to 799 patients (50.4%) in group B [Table 1]. Ethnicity did not differ significantly between both groups. More procedures in the ileitis group were performed in the morning sessions (44.4% vs. 31.3%; $P < 0.01$). Surprisingly, more patients in the ileitis group received milder sedation (34.7% vs. 21.5%).

Table 1. Baseline characteristics and endoscopic characteristics of terminal ileitis (group A) and normal ileoscopy (group B) patients

	Group A	Group B	*P* value
Number of patients	216	1584	
Age (mean ± SD) (years)	38.3 ± 17.6	42.6 ± 20	0.0001
Gender, N (%) Males Females	 123 (56.9) 93 (43.1)	 799 (50.4) 785 (49.6)	 0.03
Ethnicity, N (%) Arab Jewish	 41 (19) 175 (81)	 387 (24.4) 1197 (75.6)	 0.03
Mild sedation (benzodiazepine/opioids), N (%)	75 (34.7)	341 (21.5)	0.001
Moderate propofol sedation, N (%) < 50 mg 51–100 mg 101–150 mg > 150 mg	 4 (1.8) 16 (7.4) 19 (8.8) 49 (22.7)	 137 (8.6) 232 (14.6) 144 (9.1) 200 (12.6)	 0.0006 0.005 0.8 < 0.0001
Colonoscopy setting, N (%) Morning session Evening session	 96 (44.4) 120 (55.)	 496 (31.3) 1800 (68.7)	 0.0001
Colonoscopy findings, N (%) Pseudo-melanosis coli Polyps Colorectal cancer	 1 (0.5) 12 (5.5) 4 (1.8)	 10 (0.6) 183 (11.5) 4 (0.3)	 0.2
Sedation administered by anesthesiologist, N (%)	12 (5.5)	104 (6.5)	0.2

THE PREVALENCE OF SYMPTOMS AMONG NORMAL OF PATHOLOGICAL TI FINDINGS

Among patients with TI findings as compared to those with normal ileoscopy, more patients were referred to colonoscopy due to chronic abdominal pain and chronic diarrhea (14.4% vs. 9.3%) and for follow-up in IBD patients (44.4% vs. 10.6%), respectively. Among patients with normal ileoscopy as compared to those with TI findings, more patients were referred due to positive fecal occult blood test (FOBT) (12.7% vs. 0.9%), screening (12.4% vs. 2.5%), and constipation (12.4% vs. 5.5%) [Table 2].

CORRELATION OF CLINICAL INDICATION FOR COLONOSCOPY WITH PATHOLOGICAL TI FINDINGS

We found two main clinical indications for colonoscopy that showed significant correlation with pathological TI findings: chronic diarrhea and abdominal pain (OR 1.62, 95% confidence interval [95%CI] 1.2–2.2, $P = 0.001$) as well as follow-up procedures for IBD patients (OR 6.72, 95%CI 4.1–10.9, $P < 0.0001$) were significantly correlated with pathologic TI findings. Surprisingly, no other clinical indication had any correlation with pathologic TI findings. Indeed, the rate of TI findings were significantly lower among patients whose colonoscopies were performed due to screening purposes (OR 0.22, 95%CI 0.06–0.81, $P = 0.02$), constipation (OR 0.44, 95%CI 0.19–0.99, $P = 0.04$), and positive FOBT (OR 0.1, 95%CI 0.02–0.5, $P = 0.005$) [Table 3]. On multivariate logistic regression analysis, chronic diarrhea and abdominal pain (OR 1.96, 95%CI 1.39–2.77, $P = 0.0001$), follow-up procedures for IBD (OR 9.15, 95%CI 5.3–15.7, $P < 0.0001$), and FOBT (OR 0.11, 95%CI 0.02-0.84, $P = 0.03$) remained statistically significant correlators with pathological TI findings.

DISCUSSION

Available evidence for the performance of routine ileoscopy during colonoscopy is still equivocal, and whether TI examination impacts patient management or outcome is largely unknown [20,21]. Examination of the TI during colonoscopy is utilized as the gold standard investigation in patients with assumed TI involvement especially in cases of suspected or proven Crohn's disease patients or when abnormal imaging localizes pathology to the TI [22]. The diagnostic yield of routine TI, however, was shown to be as low as 0.3% for the screening setting and is reportedly low for other several settings [23]. Added benefit of TI intubation for common clinical scenarios such as positive FOBT or anemia has not been fully studied. Thus, the decision to intubate the TI or not is made on a case-by-case basis. Our study was designed to provide endoscopy performers with a simple, practical, and indication-based guide when and when not to intubate the TI during a given procedure particularly in a busy endoscopy schedule.

In our cohort, TI intubation was likely to be performed in a younger population, when compared to the overall age of the entire cohort. Furthermore, TI findings were more prevalent in

Table 2. Distribution of clinical indications among terminal ileum findings

Parameter	Number of patients	Pathological terminal ileum findings, N (%)	*P* value
Chronic diarrhea and abdominal pain			
Yes	954	137 (14.4)	
No	846	79 (9.3)	0.001
Follow-up after IBD patients			
Yes	72	32 (44.4)	
No	1728	184 (10.6)	< 0.001
Screening			
Yes	79	2 (2.5)	
No	1721	214 (12.4)	0.004
Constipation			
Yes	109	6 (5.5)	
No	1691	210 (12.4)	0.03
Weight loss			
Yes	84	6 (7.1)	
No	1716	210 (12.2)	0.2
Follow-up after colorectal polyps			
Yes	45	1 (2.2)	
No	1755	215 (12.2)	0.3
Anemia			
Yes	161	25 (15.5)	
No	1639	191 (11.6)	0.1
Fecal occult blood test			
Positive	103	1 (0.9)	
Negative	1697	215 (12.6)	< 0.001
Rectal bleeding			
Yes	195	20 (10.2)	
No	1605	196 (12.2)	0.4
Family history of colorectal cancer			
Yes	65	4 (6.1)	
No	1735	212 (12.2)	0.1

Table 3. parameters associated with terminal ileum findings in univariate logistic analysis

Parameter	Odds ratio	95% confidence interval	*P* value
Chronic diarrhea and abdominal pain	1.62	1.2–2.2	0.001
Follow-up in IBD patients	6.7	4.1–10.9	< 0.0001
Positive FOBT	0.1	0.02–0.5	0.005
Screening purpose	0.22	0.06–0.8	0.02
Constipation	0.44	0.2–0.9	0.04
Follow-up after polyps	0.24	0.05–1.3	0.09
Anemia	1.41	0.9–2.2	0.1
Rectal Bleeding	0.84	0.5–1.4	0.4
Family history of colorectal cancer	0.53	0.2–1.4	0.1
Weight loss	0.59	0.3–1.3	0.2

FOBT = fecal occult blood test, IBD = inflammatory bowel disease

younger ages when compared to those with normal ileoscopy. This difference may parallel the age distribution and the high frequency of IBD in the younger population. Interestingly, no noticeable gender or ethnicity characteristics were associated with the detection of TI findings. Despite several reports indicating that deeper sedation levels are associated with increased TI intubation rate [24], patients with pathologic TI findings in our cohort tended to receive milder sedations.

In the current study, the greatest yield of TI intubation was evident when applied to specific clinical conditions, namely chronic abdominal pain and diarrhea as well as in the setting of follow-up for IBDs. Our findings are in concordance with other previous studies reporting higher yields of TI intubation in similar clinical indications, supporting its performance in these settings [25].

Moreover, our study confirms the extremely low yield of ileoscopy for several other indications. One noteworthy setting is the referral of patients for colonoscopy due to positive FOBT. As a great deal of these patients may not have identifiable lesions in the colon, performing ileoscopy to search for TI lesions in this regard may be appealing. It was prudent for us to show in our study that there is a very low yield for the performance of ileoscopy in this regard. Other common indications for endoscopic evaluation in our practice include constipation. Our study showed no added value and even a negative association with TI findings in this regard, and accordingly we do not endorse TI intubation in this setting. Other indications were not significantly associated with TI findings and should be managed on a case-by-case basis. Most notably, as some procedures may be performed because of multiple indications, ileoscopy performance should be considered when the combination raises the suspicion of IBDs. In a busy schedule of endoscopic units, performing TI intubation according to the predicted yield may save valuable time and reduce work burden.

One of the strengths of our study is the high number of patients involved, as well as the inclusion of wide range of indications reflecting real world practice. Limitations of our study are inherent in its single-center and retrospective design. Moreover, some procedures were performed because of multiple indications and this may have impacted the statistical analyses.

CONCLUSIONS

TI intubation may have a higher yield when performed in the setting of chronic abdominal pain and diarrhea investigation, may be superfluous in patients referred for constipation or positive FOBT, and should be performed in case-by-case basis for other indications.

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