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Original Article

The effect of routine terminal ileal intubation on conventional colonoscopy without specific indications

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Abstract: Backgrounds: Colorectal cancer (CRC) can be prevented and drastically reduced with colonoscopy. Whether Terminal ileal intubation (TII) is necessary for routine colonoscopy, and whether TII affects the adenoma detection rate (ADR) and the polyp detection rate (PDR), there is currently a lack of prospective studies. Methods: We retrospectively collected and analyzed data from patients who underwent colonoscopy at our hospital from June 1, 2020 to March 20, 2021, to evaluate the detection rate of intestine diseases diagnosed by TII, and to find factors related to ADR and PDR. Results: Among the 398 patients who completed cecal intubation (CI), TII was performed in a total of 207 cases (51.76%, 207/398), and no intestinal diseases were found. On univariable analysis, the TII/non-TII had no significant influence on PDR (49.8% vs. 57.6%, P>0.05) and ADR (30.4% vs. 28.8%, P>0.05). On multivariable analysis, Age, Sex, and colonoscopy withdrawal time (CWT) were independent positive predictors of polyps, while Age, Tobacco Use, and A.M. procedure were independent positive predictors of adenoma. Conclusion: These results highlighted Age and Sex as important risk factors for polyps and adenomas, and CWT as an important parameter to improve PDR and ADR. Meanwhile, the incidence of intestine disease was low in colonoscopy screening cases, where TII cannot improve the detection rate of intestinal disease nor help to improve ADR and PDR. Considering its cost-effectiveness, and the low prevalence of intestine disease, there is no clear evidence for the need to increase TII in routine colonoscopy without specific indications. We need to focus our limited efforts on factors that make sense for improving PDR and ADR, such as paying attention to male and senior patients and adequate CWT.

Keywords: Adenoma detection rate, colonoscopy, colorectal cancer, polyp detection rate, terminal ileal intubation

Introduction

Globally, colorectal cancer (CRC) is the third most common cancer and the fourth leading cause of death from cancer [1]. It has become a global public health issue that affects patients, healthcare systems, and society in a substantial way. In screening colonoscopies, CRC is detected, and premalignant neoplasms at risk of advancing to CRC are identified and eliminated [2]. The absolute risk of CRC can be drastically reduced by a colonoscopy, according to a large population-based study [3]. As colonoscopy screenings become more prevalent nationwide, it is increasingly important to ensure that all endoscopists and endoscopy units perform at a high level. The clear and concise colonoscopy quality indicators, which include the bowel preparation quality, cecal intubation rate (CIR), colonoscopy withdrawal time (CWT), adenoma detection rate (ADR) and polyp detection rate (PDR), are the guarantee of highly efficient screening and good patient outcomes [4, 5].

Terminal ileal intubation (TII) is a common technique used in colonoscopy. For cases with atypical ileocecal structures, TII ensures the integrity of the colon mucosal examination. A TII may also be required for patients with specific indications, such as inflammatory bowel disease, colonic lymphoma, or lower gastrointestinal bleeding [6, 7]. The reported terminal ileal intubation rate (TIIR) varies among different cohorts [6]. A successful TII, which means fully straightening the colonscopy and reaching the deep part of Terminal ileal (TI) with the skilled endoscopic technique, satisfactory bowel prepara-

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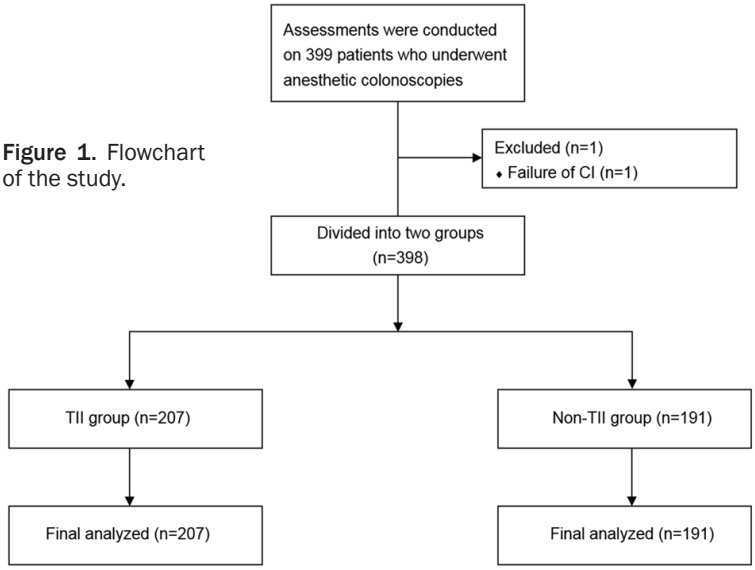

Figure 1. Flowchart of the study.

tion, well tolerance of patient, and more adequate observation of TI, lead to excessive consumption of limited energy of endoscopists. At present, limited studies have not yet made clear whether such extra efforts can yield returns such as increased CRC and pre-malignant neoplasm detection. This study aims to retrospectively analyze the impact of TII on the quality of colonoscopy, specifically focusing on the effects on ADR and PDR.

Materials and methods

Patients

The study was open to all patients aged 18 and older who underwent anesthetic colonoscopy at Shanghai Tongren Hospital between July 1, 2020 and March 20, 2021. The study excluded patients who had previously undergone colorectal surgery or endoscopic treatment. TII cases were enrolled in the TII group, followed by age- and sex-matched cases without TII enrolled in the non-TII group (**Figure 1**). Age, sex, body mass index (BMI), colonoscopy indications, smoking status, past medical history (PMH), and family history were recorded as clinical variables. Each patient signed a written informed consent to participate in the study. Shanghai Tongren Hospital's Institutional Review Board approved the study. Trial information can be found at http://www.chictr.org.cn (ID: ChiCTR2100048292).

Colonoscopy

Bowel preparation with laxatives such as polyethylene glycol electrolytes and magnesium sodium potassium sulfate was routinely administered prior to colonoscopy. Senior endoscopists performed all colonoscopy procedures. The TII group required TII, while the non-TII group only needed cecal intubation (CI). According to previous research [7], the exact time of the colonoscopy was recorded, which included the beginning time, the CI time, the TII time, the mean time from CI to arrival at the deep part of TI mucosa, the depth of TI terminal mucosa, and CWT was calculated from the time of colonoscopy withdrawing from cecum to anal canal without biopsy or therapeutic procedures. For the high quality of bowel cleaning, a water pump was used during the colonoscopy [8]. We make the initial diagnosis based on the morphologic features of the lesion under colonoscopy and make the final diagnosis based on biopsy pathology, such as inflammation, hyperplasia, adenoma, and carcinoma.

Indications

Indications for patients undergoing colonoscopy include Blood in the stool, abdominal pain, diarrhea, constipation, changes in bowel habits, increased serum tumor marker concentrations, weight loss, and screening for asymptomatic individuals. To simplify the analysis, the indications were divided into asymptomatic and symptomatic.

Outcomes

ADR and PDR were the primary outcomes. The secondary outcome included procedure time, which was classified as the a.m. and p.m. colonoscopy based on the cut-off time point of 12:00 hours. In addition, the Boston bowel preparation scale (BBPS) was used to score the quality of bowel preparation, and BBPS scores of six or more and segment scores of two help define adequate [9, 10].

Table 1. Clinical characteristics of colonoscopy cases by terminal ileum intubation

Patients (n=398)	Overall (N=398)	TII (N=207)	Non-TII (N=191)	*P*-value
Age, mean ± sd, years	53.40±11.69	53.41±11.87	53.39±11.55	0.991
Male	213 (53.5%)	105 (50.7%)	108 (56.5%)	0.245
BMI, mean ± sd	23.99±3.41	23.74±3.18	24.26±3.64	0.130
Tobacco Use	95 (23.9%)	44 (21.3%)	51 (26.7%)	0.203
Indications				
Asymptomatic	153 (38.4%)	79 (19.8%)	74 (18.6%)	0.903
Hematochezia	50 (12.6%)	29 (14.0%)	21 (11.0%)	0.365
Diarrhea	49 (12.3%)	21 (10.1%)	28 (14.7%)	0.171
Constipation	40 (10.1%)	25 (12.1%)	15 (7.9%)	0.161
Changes in bowel habits	46 (11.6%)	23 (11.1%)	23 (12%)	0.772
Bellyache	63 (15.8%)	31 (15.0%)	32 (16.8%)	0.627
Increased serum tumor markers	18 (4.5%)	8 (3.9%)	10 (5.2%)	0.677
Weight loss	4 (1.0%)	2 (1.0%)	2 (1.0%)	1.000
PMH				
HBP	71 (17.8%)	31 (15.0%)	40 (20.9%)	0.120
DM	32 (8.0%)	17 (8.2%)	15 (7.9%)	0.895
FLD	32 (8.0%)	13 (6.3%)	19 (9.9%)	0.179
Hyperlipidemia	17 (4.3%)	6 (2.9%)	11 (5.8%)	0.159
Family history of cancer	44 (11.1%)	20 (9.7%)	24 (12.6%)	0.356
Procedural characteristics				
Time of the day (A.M.)	149 (37.4%)	87 (42.0%)	62 (32.5%)	0.049
BBPS score, mean ± Sd	8.17±1.13	8.26±1.08	8.07±1.18	0.090
Time of CI, mean ± Sd, seconds	223.21±104.26	230.94±110.00	214.87±97.56	0.125
CWT, mean ± Sd, seconds	362±36.78	361.96±37.13	362.04±36.60	0.983

BBPS: Boston bowel preparation scale system; BMI: Body Mass Index; CI: cecum intubation; CWT: colonoscopy withdrawal time; DM: Diabetes Mellitus; FLD: fatty liver disease; HBP: High blood pressure; PMH: Past Medical History; SD: standard deviation; TII: terminal ileum intubation.

Statistical analysis

As a result of the normality test of time to CI, a *p*-value of 0.05 was obtained, indicating that the distribution was skewed. Thus, Wilcoxon rank sum test was applied to compare the time to reach the cecum between TI intubation and non-TI intubation. Using stepwise selected logistic regression analysis, the factors associated with *p*-values less than 0.05 in the univariate analysis were subjected to multivariate analysis. Statistical significance was defined as a *p*-value of less than 0.05. SPSS 24.0 (IBM, Chicago, USA) was used to perform all analyses.

Results

There were 399 colonoscopy cases included in this study; the overall CIR (398/399) was 99.75%. There was only one case which was excluded due to the failure of CI for tumor obstruction. No bleeding, perforation and other serious complications were reported. In patients with CI, 53.7% were male (n=213), the mean age was 53.40±11.69 years, and the mean BMI was 23.99±3.41. One hundred percent of patients received adequate bowel preparation. The mean CI time was 223.21±104.26 seconds. TII was performed in a total of 207 cases (51.76%, 207/398), In the TII group, TIIR was 100%, and TII depth reached 40 cm maximum. A mean time of 46.26±34.76 seconds was observed for TII, and 37.05±20.91 seconds were observed for CI in the deep part of TI mucosa (**Table 1**). Intestinal disease cases were not detected. The overall PDR was 53.52% (213/398), and the ADR was 29.65% (118/398). High-grade adenoma, low-grade adenoma, hyperplastic polyps, and neuroendocrine tumors (NETs) were detected at 1.76% (7/398), 27.89% (111/398), 23.62% (94/398),

Table 2. Using univariate analysis, polyp detection rates were correlated with study variables

Demographics	Polyps+ (n=213)	Polyps- (n=185)	*P*-value
Age, mean ± Sd (years)	56.67±11.11	49.63±11.25	<0.001
Male	128 (60.1%)	85 (39.9%)	<0.005
BMI	24.258±3.40	23.69±3.41	0.098
Tobacco Use	66 (69.5%)	29 (30.5%)	<0.001
Indications			
Asymptomatic	88 (57.5%)	65 (42.5%)	0.206
Symptomatic	125 (51.0%)	120 (49.0%)	
Hematochezia	27 (54.0%)	23 (46.0%)	0.942
Diarrhea	24 (49.0%)	25 (51.0%)	0.496
Constipation	15 (37.5%)	25 (62.5%)	0.032
Changes in bowel habits	24 (52.2%)	22 (47.8%)	0.846
Bellyache	37 (58.7%)	26 (41.3%)	0.366
Increased serum tumor markers	10 (55.6%)	8 (44.4%)	0.859
Weight loss	2 (50.0%)	2 (50.0%)	1.000
PMH			
HBP	46 (64.8%)	25 (35.2%)	0.036
DM	17 (53.1%)	15 (46.9%)	0.963
FLD	18 (56.3%)	14 (43.7%)	0.747
Hyperlipidemia	11 (64.7%)	6 (35.3%)	0.345
Family history of cancer	22 (50.0%)	22 (50.0%)	0.620
Procedural characteristics			
TII	103 (49.8%)	104 (50.2%)	0.118
BBPS score, mean ± Sd	8.11±1.1961	8.23±1.06	0.294
Time of the day (A.M.)	88 (59.1%)	61 (40.9%)	0.086
Time of CI, mean ± Sd	226.49±103.95	219.47±105.06	0.504
CWT, mean ± Sd	367.83±38.64	355.29±33.49	0.001

On univariable analysis, age, male sex, Tobacco use, Constipation, HBP and longer CWT were associated with higher PDR. BBPS: Boston bowel preparation scale system; BMI: Body Mass Index; CI: cecum intubation; CWT: colonoscopy withdrawal time; DM: Diabetes Mellitus; FLD: fatty liver disease; HBP: High blood pressure; PMH: Past Medical History; SD: standard deviation; TII: terminal ileum intubation.

and 0.25% (1/398), respectively. In order to observe whether TII affects the ADR and PDR, we first evaluated the baselines of the two groups. Based on **Table 1**, no difference was found between the TII and non-TII groups in clinical characteristics (P>0.05).

As determined by univariable analysis, older age, male sex, longer CWT, tobacco use, constipation, and higher HBP were associated with higher PDR (P<0.05), but TII and non-TII did not play a significant role (49.8% and 57.6%, respectively, P>0.05, **Table 2**). Meanwhile, older age, tobacco use, time of the day for colonoscopy (A.M.), longer CI time, and HBP were associated with higher ADR (P<0.05), and TII vs non-TII had no significant influence on ADR (30.4% vs. 28.8%, P>0.05, **Table 3**). Further multivariable analysis found that Age, Sex, and CWT were independent predictors of positive polyp findings, and Age, Tobacco Use, and A.M. procedure were independent predictors of positive adenoma findings (**Table 4**).

Discussion

TII under colonoscopy can help diagnose intestine diseases in the TI, but the incidence of intestine diseases is relatively low [11]. When TII was applied as part of a routine colonoscopy, it had a low yield of finding intestine diseases [12]. Our previous study results also showed that the diagnosis rate of intestine disease is only 1%, which can explain why there were no intestine disease findings in the 201 TII cases in this study.

Table 3. A univariable analysis revealed a correlation between study variables and the rate of adenoma detection

Demographics	Adenomas (n=118)	No adenomas (n=280)	*P*-value
Age, mean ± Sd (years)	57.52±11.35	51.67±11.43	<0.001
Male	72 (33.8%)	141 (66.2%)	0.051
BMI	24.50±3.65	23.78±3.29	0.053
Tobacco Use	42 (44.2%)	53 (55.8%)	<0.001
Indications			
Asymptomatic	88 (57.5%)	65 (42.5%)	0.206
Symptomatic	125 (51.0%)	120 (49.0%)	
Hematochezia	18 (36.0%)	32 (64.0%)	0.293
Diarrhea	13 (26.5%)	36 (73.5%)	0.610
Constipation	9 (22.5%)	31 (77.5%)	0.297
Changes in bowel habits	13 (28.3%)	33 (71.7%)	0.827
Bellyache	18 (28.6%)	45 (71.4%)	0.838
Increased serum tumor markers	7 (38.9%)	11 (61.1%)	0.859
Weight loss	1 (25.0%)	3 (75.0%)	1.000
PMH (Past Medical History)			
HBP	28 (39.4%)	43 (60.6%)	0.046
DM	9 (28.1%)	23 (71.9%)	0.844
FLD	11 (34.4%)	21 (65.6%)	0.542
Hyperlipidemia	8 (47.1%)	9 (52.9%)	0.108
Family history of cancer	13 (29.5%)	31 (70.5%)	0.987
Procedural characteristics			
TII	63 (30.4%)	144 (69.6%)	0.721
BBPS score, mean ± Sd	8.15±1.22	8.18±1.09	0.857
Time of the day (A.M.)	55 (36.9%)	94 (63.1%)	0.014
Time of CI, mean ± Sd	245.35±118.05	213.91±96.80	0.006
CWT, mean ± Sd	367.18±38.67	359.82±35.87	0.069

On univariable analysis, age, Tobacco Use, HBP, AM procedure, and long CI time were associated with higher PDR. BBPS: Boston bowel preparation scale system; BMI: Body Mass Index; CI: cecum intubation; CWT: colonoscopy withdrawal time; DM: Diabetes Mellitus; FLD: fatty liver disease; HBP: High blood pressure; PMH: Past Medical History; SD: standard deviation; TII: terminal ileum intubation.

Table 4. A multivariable analysis identified factors associated with polyp and adenoma detection rates

	OR	95% CI	*P*-value
Factors in PDR			
Age	1.063	1.043-1.085	0.000
Sex	0.447	0.288-0.692	0.000
CWT	1.011	1.003-1.018	0.000
Factors in ADR			
Age	1.042	1.021-1.064	0.000
Tobacco Use	2.334	1.416-3.847	0.000
A.M. procedure	0.620	0.391-0.983	0.042

Multivariable analysis indicated that Age, Sex, and CWT were independent positive predictors of polyp, and Age, Tobacco Use, and AM procedure were independent positive predictors of adenoma. CI: confidence interval; CWT: colonoscopy withdrawal time; OR: odds ratio.

The CI was a marker for the integrity of colonoscopy, and it was correlated with both ADR and PDR [13, 14]. In our research, with the help of adequate bowel preparation, efficient sedation, and anesthesia, we have achieved 100% CIR by observing the ileocecal area and appendix orifice. There was no need for TII to confirm the CI. This result was consistent with our previous retrospective studies. Therefore, it is unnecessary to use TII to help confirm completion in screening colonoscopy, only when the structural features of the cecum are ambiguous or altered, such as insufficient bowel preparation, after colon surgery, after ileocecal lesions, etc.

It has been shown that screening for CRC reduces women's and men's average cancer mortality risk [3, 15]. The American Cancer

Society (ACS) recommends that following regular high-sensitivity stool-based screening or a structural (visual) examination, all positive non-colonoscopy screening tests should be followed up with colonoscopy in a timely manner [16]. As a result, screening colonoscopy is particularly important in the process of CRC screening. The ADR is the most direct quality indicator to evaluate the quality of colonoscopy [17, 18]. No need to wait for pathological results, PDR can be obtained directly through endoscope, and ADR can be accurately estimated by using the quotient of adenoma to PDR [19]. Other key quality indicators, such as CIR (minimum standard: ≥90%), rate of adequate bowel preparation (minimum standard: ≥90%), CWT (minimum standard: mean 6 min), are the guarantee of the ideal ADR (minimum standard: ≥25%) and PDR (minimum standard: ≥40%) [8, 20].

Pursuing to higher ADR and PDR might mean better reduction of CRC morbidity and fatality through a variety of approaches, such as improving bowel cleaning efficiency, cap-assisted colonoscopy (CAC), endocuff vision (EV) of colonoscopy, or the incorporation of artificial intelligence in endoscopy, etc. [21-24]. For the majority of primary medical institutions, what can be done is to work according to the existing conditions of endoscopy unit and follow the consensus guidelines, and to improve their own endoscopic techniques constantly. Proficient endoscopic techniques represent a higher colonoscopy completion rate. As part of simple techniques, it is important to ensure adequate bowel preparation, proper sedation, and sufficient time to complete a problematic colonoscopy. A recent study showed that skilled endoscopic techniques were associated with higher ADR and TIIR [25].

In order to observe the possible impact of TII on ADR and PDR, this study strictly maintained adequate bowel preparation in accordance with the guidelines, cooperated with anesthesia recommendations, ensured 100% of CIR and TIIR and provided sufficient CWT to accurately detect adenomatous lesions and ensure the overall ADR and PDR were significantly higher than our previous study (27% in PDR, 17% in ADR) without any complications [7]. We found that the improved ADR and PDR were statistically independent of TII. In previous retrospective studies [7, 26], random TII cases may be more appropriate for younger, lower BMI and less difficulty colonoscopy patients, and these cases may have polyp incidences which are relatively low, so the results showed that TII was not correlated with ADR or was negatively correlated with PDR. Compared with our study, we ruled out those factors that may cause a bias. In addition, with the improvement of intestinal cleanliness, PDR, and ADR, the results suggest that routine TII in colonoscopy screening cannot improve PDR and ADR.

The risk factors for colorectal polyps encompass age, gender, smoking, obesity, alcohol, physical activity, dietary factors, etc. [27]. In this study, the multivariate analysis showed that age, gender, and smoking were independent influencing factors of PDR or ADR, long CWT helped to improve polyp detection, which are consistent with previous studies. The A.M. procedure helps to improve ADR; considering the small sample size at this time, this factor needs further research and discussion in the future. In general terms, while the sample size was limited, it still revealed the objective feature. Considering cost-effectiveness of screening colonoscopy and the low prevalence of intestinal disease, there was no clear evidence for the need to add TII to routine colonoscopy without a specific indication. We need to focus our limited efforts on factors that have a meaningful impact on improving PDR and ADR, such as age, gender, and CWT.

While interpreting the results, there were some limitations of our study which may be considered. The first disadvantage of our study is that it was a small sample size study carried out in one center, which means that the results cannot be generalized to all settings. Secondly, the participants in our research were all senior endoscopists. This study failed to show whether TII practice was helpful for the growth of endoscopy skills of junior endoscopists and the improvement of ADR and PDR. New clinical research can be designed to address this in the future.

Conclusion

In our retrospective cohort database, compared with CI, TII, with consumption of extra time and effort, cannot improve ADR, PDR, and increase intestinal pathology diagnosis in conventional colonoscopy without specific indica-

tions. Combined with our previous retrospective study results, we suggest that TII should not be routinely performed during conventional colonoscopy without specific indications. Together, our limited efforts must be focused on essential elements for improving PDR and ADR, such as paying attention to male and senior patients and adequate CWT.

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Disclosure of conflict of interest

None.

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