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Retrospective Study

Impact of looping on premalignant polyp detection during colonoscopy

Toyoshima O *et al*. Looping on adenoma detection during colonoscopy

Abstract

BACKGROUND

The presence of premalignant polyps on colonoscopy is an indicator of metachronous colorectal cancer. Looping during colonoscopy is associated with old age, female sex, and colonoscopy insertion time. However, the clinical significance of looping is not fully understood. We aimed to clarify the effect of looping on colorectal premalignant polyp detection.

AIM

To assess the effects of looping on premalignant polyp detection using logistic regression analyses.

METHODS

We retrospectively investigated patients who underwent colonoscopy at Toyoshima Endoscopy Clinic between May, 2017 and October, 2020. From the clinic's endoscopy database, we extracted data on patient age, sex, endoscopist-assessed looping, colonoscopy duration, endoscopist experience, detection rate, and number of premalignant polyps.

RESULTS

We assessed 12259 patients (mean age, 53.6 years; men, 50.7%). Looping occurred in 54.3% of the patients. Mild and severe looping were noted in 4399 and 2253 patients, respectively. The detection rates of adenomas, advanced adenomas, high-risk adenomas, clinically significant serrated polyps (CSSPs), and sessile serrated lesions (SSLs) were 44.7%, 2.0%, 9.9%, 8.9%, and 3.5%, respectively. The mean numbers of adenomas and SSLs were 0.82 and 0.04, respectively. The detection rates of adenomas, high-risk adenomas, and CSSPs increased with looping severity (all $P < 0.001$). The number of adenomas increased with looping severity ($P < 0.001$). Multivariate analyses found that detection of adenomas, high-risk adenomas, and CSSPs was associated with

severe looping ($P < 0.001$, $P < 0.001$, and $P = 0.007$, respectively) regardless of age, sex, time required for colonoscope insertion and withdrawal, and endoscopist experience.

CONCLUSION
Looping severity was independently associated with high detection rates of premalignant polyps. Therefore, looping may predict the risk of metachronous colorectal cancer. Endoscopists should carefully examine the colorectum of patients with looping.

Key Words: Looping; Colorectal polyp; Colonoscopy; Adenoma; Serrated polyp; Colorectal neoplasm

Core Tip: This study aimed to clarify the effect of colonic looping on colorectal premalignant polyp detection during colonoscopy. We retrospectively investigated 12259 patients who underwent colonoscopies. Looping occurred in 54.3% (35.9% and 18.4% with mild and severe looping, respectively) of the cases. The detection rates of adenomas (44.7%), high-risk adenomas (9.9%), and clinically significant serrated polyps (CSSPs) (8.9%) increased with the looping severity. The number of adenomas per colonoscopy (0.82) increased with the looping severity. Multivariate analyses found that detection of adenomas, high-risk adenomas, and CSSPs was associated with severe looping regardless of age, sex, time required for colonoscope insertion and withdrawal, and endoscopist experience.

INTRODUCTION

Colorectal cancer mainly occurs because of adenomas or serrated polyps[1-3]. Colonoscopy is the gold standard for cancer screening and detection of premalignant polyps. The prevalence of metachronous colorectal cancer is high in patients with adenomas, especially high-risk adenomas, removed during colonoscopy[4]. Similarly, individuals with colonoscopically resected clinically significant serrated polyps (CSSPs) have a long-term risk of colorectal cancer[5-7]. Thus, the detection of adenomas and CSSPs on colonoscopy is a surrogate marker for the risk of metachronous colorectal cancer. Factors related to premalignant polyp detection include patient characteristics, such as age and sex[8,9], and endoscopic procedure-related factors, such as cecal intubation time[10], withdrawal time[11-14], and endoscopist experience[8].

Colonic looping is a common obstacle during routine colonoscopy[15,16]. Looping is associated with a redundant colon, older age, female sex, and cecal intubation time[17-20]. However, the clinical significance of looping is poorly understood. Therefore, this study aimed to clarify the effect of looping on colorectal premalignant polyp detection by using multivariate analysis to control for potential confounding factors.

MATERIALS AND METHODS

Study design and overview

This retrospective study was conducted at a single institute, Toyoshima Endoscopy Clinic, a representative outpatient endoscopy-specialized clinic located in an urban area of Japan. Toyoshima Endoscopy Clinic performs 10000 endoscopies annually. The study design was described in a protocol prepared at Toyoshima Endoscopy Clinic and approved by the Certified Institutional Review Board of Yoyogi Mental Clinic on July 16, 2021 (Approval no. RKK227). We published this study's protocol on our institute's website (www.ichou.com). Thus, patients could opt out of the study if desired. Written informed consent for the use of clinical information was obtained before the colonoscopy. All the authors approved the final manuscript. No funding was received for this study.

Patients

Patients who underwent colonoscopy at Toyoshima Endoscopy Clinic between May, 2017 and October, 2020 were enrolled in this study. The indications for colonoscopy included the examination of symptoms and abnormal findings, screening, and surveillance for colorectal diseases. Patients undergoing treatment, such as polypectomy and hemostasis, those with poor bowel preparation[21,22], and those with a history of colorectal surgery were excluded. Cases of colonoscopies with incomplete cecal intubation, withdrawal time of < 6 min[11], and those performed with an ultrathin colonoscope[23] were also excluded.

Definition of looping

Common colonic looping patterns observed during colonoscopy have been described previously. Loops occur in the transverse and sigmoid colons, and sigmoid loops include alpha and N shapes[19,24]. When forming a loop, there is no one-to-one relationship between the transmission of the colonoscope shaft movement and colonoscope tip motion. In the case of looping, further insertion of the scope results in a larger loop size without de-looping the scope[24,25].

Cecal insertion without loop formation was defined as the absence of looping. Cecal insertion that required straightening of the colonic loop once was defined as mild looping. Cecal insertion that required straightening of the colonic loop two or more times was defined as severe looping.

Colonoscopy

Small and gentle shaking and jiggling of the colonoscope shaft were performed. Right-turn shortening maneuvers for straightening the shaft were used for colonoscope insertion. Water-assisted, carbon dioxide-assisted, and cap-assisted chromoendoscopies with sedation were performed[26]. Position changes and rectal retroflexion were performed[8,27]. When looping was formed, we usually controlled the colonoscope by

changing the patient's position to supine or right lateral, and manual abdominal compression was performed by the assistant[15].

Thirty endoscopists with various levels of experience performed the colonoscopies[28,29]. This study defined experienced endoscopists as those with > 15 years of experience in performing endoscopy. We used a combination of the Elite system and CF-HQ290ZI, CF-HQ290I, or PCF-H290ZI colonoscopes (Olympus Corporation, Tokyo, Japan). Poor bowel preparation was defined as at least one colon segment that could not be examined because of the presence of remnant solid stool[9,16,27].

Colorectal polyps

All polyps suspected to be cancerous, adenomatous, or CSSP were removed or biopsied. All polyps were histologically diagnosed by an experienced gastrointestinal pathologist using the resected specimens and biopsy samples. Advanced adenomas included adenomas ≥ 10 mm in size, villous adenomas, and adenomas with high-grade dysplasia. A high-risk adenoma was defined as the presence of advanced adenoma and/or three or more adenomas. CSSPs comprise all sessile serrated lesions (SSLs), all traditional serrated adenomas, hyperplastic polyps of size ≥ 10 mm anywhere in the colorectum, and hyperplastic polyps of size ≥ 5 mm located between the cecum and descending colon[30-33].

Outcomes

We extracted data from the endoscopy database of Toyoshima Endoscopy Clinic, including patient age, sex, endoscopist-assessed looping, colonoscope insertion time, withdrawal time, endoscopists, detection rates of adenomas, advanced adenomas, high-risk adenomas, CSSPs, and SSLs, and numbers of adenomas and SSLs. Withdrawal time was defined as the time required to examine the colorectal mucosa and remove the polyps. The polyp detection rate was defined as the rate of colonoscopies that detected at least one polyp.

Statistical analysis

The significance of any orderly increase or decrease along the three stratifications (*i.e.*, no, mild, and severe looping) was assessed using Cochran-Armitage trend test or Jonckheere-Terpstra trend test for categorical and continuous variables, respectively. Because of the significant association between looping severity and polyp detection in the trend test, the effect of subject characteristics on polyp detection was analyzed using a multivariate analysis. Furthermore, a subgroup analysis, limited to experienced endoscopists, was performed. Multivariate analysis was performed using a binomial logistic regression model, with no, mild, and severe looping scores of 0, 1, and 2, respectively. Statistical significance was defined as a *P*-value < 0.05. The calculations were performed using Bell Curve for Excel version 3.22 (Social Survey Research Information Co., Ltd., Tokyo, Japan) and R version 4.1.2 (R Core Team 2021, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Patients

During the study period, colonoscopies were performed on 13315 patients. We excluded 236 patients undergoing treatment, such as polypectomy and hemostasis, 77 with poor bowel preparation, 217 with previous colorectal surgery, 20 with incomplete cecal insertion (including 8 with stenosis caused by colorectal tumor and 6 with colonic looping), 22 with withdrawal time < 6 min, and 484 who were examined using an ultrathin colonoscope. Ultimately, 12259 patients were enrolled in this study. A patient flowchart is shown in Figure 1.

The mean patient age was 53.6 years. Men accounted for 50.7% of the participants. Looping occurred in 54.3% of the patients. There were 4399 and 2253 patients with mild and severe looping, respectively. The mean insertion and withdrawal times were 4.6 and 13.9 min, respectively. Experienced endoscopists performed 70.4% of the colonoscopies. The polyp detection rates for adenomas, advanced adenomas, high-risk

adenomas, CSSPs, and SSLs were 44.7%, 2.0%, 9.9%, 8.9%, and 3.5%, respectively. The mean number of adenomas and SSLs was 0.82 and 0.04, respectively (Table 1).

Subject characteristics based on looping
Patients with severe looping tended to be older and more likely to be female (both $P < 0.001$). Cecal insertion and withdrawal times tended to be longer in severe looping (both $P < 0.001$). Experienced endoscopists performed cases with severe looping more often. The polyp detection rates of adenomas ($P < 0.001$), advanced adenomas, high-risk adenomas ($P < 0.001$), CSSPs ($P < 0.001$), and SSLs tended to increase with looping severity. However, the tendency of advanced adenoma and SSL detection rates were not statistically significant ($P = 0.166$ and $P = 0.064$, respectively). The number of adenomas increased with looping severity ($P < 0.001$, Table 2).

Multivariate analysis of effect on polyp detection
We investigated the effect of subject characteristics on the detection of adenomas, high-risk adenomas, and CSSPs using multivariate analyses. The detection of adenomas and high-risk adenomas was independently associated with severe looping (both $P < 0.001$), old age, male sex, short insertion time, long withdrawal time, and endoscopist experience. CSSP detection was independently associated with severe looping ($P = 0.007$), female sex, short insertion time, long withdrawal time, and endoscopist experience (Table 3).

Subgroup analysis limited to experienced endoscopists
We performed a subgroup analysis that was limited to experienced endoscopists. Multivariate analyses showed similar results to the all-case analyses, that is, severe looping was independently associated with high detection rates of adenomas, high-risk adenomas, and CSSPs ($P < 0.001$, $P < 0.001$, and $P = 0.008$, respectively; Table 4).

DISCUSSION

In this study, we found that the severity of looping during colonoscopy was positively associated with high detection rates of adenomas, high-risk adenomas, and CSSPs, independent of other confounding factors, such as patient age, sex, colonoscope insertion and withdrawal times, and endoscopist experience. To the best of our knowledge, this is the first study to demonstrate a relationship between looping and polyp detection. Adenomas, high-risk adenomas, and CSSPs are precancerous lesions[2]. Recent studies have also shown that adenoma, high-risk adenoma, and CSSP detection rates are associated with a high risk of metachronous colorectal cancer[4,6]. Therefore, looping may predict a high frequency of metachronous colorectal cancer; however, further analysis is needed. Colonoscopists should carefully examine the colorectal region of patients with looping considering the high premalignant polyp detection rate.

Magnetic endoscopic imaging, computed tomographic colonoscopy, and autopsy revealed that looping was more common in older adults and women. Loop formation is also associated with prolonged cecal insertion time[17-20]. In our study, looping severity was associated with older age, female sex, and longer insertion time. Our results were consistent with those of previous studies. Looping during colonoscopy mainly occurs in the intraperitoneal segments of the colon, such as the transverse and sigmoid colon[15,17,19,20,34,35]. Barium enema and computed tomographic colonoscopy revealed that older adults and women had longer colons and larger colonic surface areas than younger adults and men, respectively. Differences in the total length and surface area are predominantly due to differences in the transverse colon[36-38]. The increased length and surface area of the colon may contribute to the formation of loops and high frequency of premalignant polyps.

Colonic redundancy is a major cause of looping during colonoscopy[39]. Colonic elongation and tortuosity appear to be related to redundancy of the colon, such as in the transverse and sigmoid colon[40,41]. Older adults and women often present with colonic redundancy and looping[41]. Raahave *et al*[42] reported that colonic transit time is associated with redundant colonic loops. Constipation increases the risk of colorectal

cancer[43]. This causes prolonged contact between the colonic mucosa and carcinogens in the stool.

Our study showed that adenoma detection was associated with old age, male sex, short insertion time, long withdrawal time, and endoscopist experience. These results are consistent with those of previous studies[8,10-12]. Female sex and longer withdrawal time, but not older age, were associated with CSSPs in our study. These findings are also concordant with those of previous studies[44-46]. The consistency of these results strengthens the credibility of this study.

Limitations

This study had several limitations. First, this study was retrospectively conducted at a single institution; however, medical data were well-controlled. Second, although patients' body mass index, family history of colorectal cancer, and gynecological surgery are associated with the presence of premalignant polyps and looping[25,47], they were not examined. Third, since mucosal exposure can affect adenoma detection rate[48], the shape of looping, de-looping method, and successful de-looping after cecal intubation should be evaluated, not only the degree of looping during insertion. However, our data do not contain this information. Further verification is required in the future.

CONCLUSION

In conclusion, the severity of looping during colonoscopy was strongly associated with high detection rates of premalignant polyps, such as adenomas, high-risk adenomas, and CSSPs. Therefore, looping may predict the risk of metachronous colorectal cancer; however, further investigation is needed. Endoscopists should be more careful when examining for colorectal polyps in patients with looping.

ARTICLE HIGHLIGHTS

Research background

Colonic looping is a common obstacle during routine colonoscopy.

Research motivation

Looping is associated with a redundant colon, older age, female sex, and cecal intubation time. However, the clinical significance of looping is not fully understood.

Research objectives

We aimed to clarify the effect of looping on colorectal premalignant polyp detection.

Research methods

We extracted data from the clinic's endoscopy database on patient age, sex, endoscopist-assessed looping, colonoscopy duration, and premalignant polyp detection. The effects of looping on premalignant polyp detection were assessed using logistic regression analyses.

Research results

The detection rates of adenomas, high-risk adenomas, and CSSP increased with the severity of looping (all $P < 0.001$). The number of adenomas increased with looping severity ($P < 0.001$). Multivariate analyses found that detection of adenoma, high-risk adenoma, and CSSP was associated with severe looping regardless of age, sex, and the time required for colonoscope insertion and withdrawal, and endoscopist's experience ($P < 0.001$, $P < 0.001$, and $P = 0.007$, respectively).

Research conclusions

Looping severity was independently associated with high detection rates of premalignant polyps.

Research perspectives

Looping may predict the risk of metachronous colorectal cancer; however, further investigation is needed.

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