Adherence to Recommendations and Quality of Endoscopic Colorectal Cancer Surveillance in Long-Standing Ulcerative Colitis

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Keywords

Colonoscopy · Colorectal cancer · Early detection ·
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Abstract

Background: Long-standing ulcerative colitis has been associated with an increased risk of colorectal cancer (CRC). Current guidelines recommend endoscopic CRC screening after 8 years of disease duration. The objectives of our study were to assess the adherence to recommendations and the quality of endoscopic procedure in long-standing ulcerative colitis. **Methods:** This is a retrospective cohort study. We selected patients included in the Swiss IBD cohort with a disease duration of ≥ 8 years and an extension above the rectosigmoid junction. The complementary medical chart review focused on endoscopy and associated histological reports in 8 Swiss centers. Descriptive analyses focused on patients and their colonoscopies. **Results:** 309 colonoscopies were conducted among 116 patients with the following characteristics: women 47%, mean age at diagnosis 31 years, and pancolitis disease extent in 65.5% of cases; 38.8% of patients had a first screening colonoscopy < 8 years, 13.8% between 8 and 10 years, and 47.4% > 10 years. Cecal intubation was

performed in 94.5% of cases, and bowel preparation was good to excellent in 61.5% of endoscopies. Chromoendoscopy was used in 7.4% of cases, and the mean withdrawal time was 16.4 min. Dysplasia was found in 6.2% of cases. **Conclusion:** Despite current international recommendations, a significant number of patients did not receive a proper endoscopic surveillance. An increased use of chromoendoscopy, monitoring of withdrawal time, and appropriate bowel preparation would increase the quality of CRC screening. The adherence to screening guidelines and endoscopic quality should be promoted and standardized.

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Introduction

Colorectal cancer (CRC) is estimated to affect 5–6% of the global population in Europe and the USA. The incidence in Switzerland is around 4,000 new cases/year, and

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it is considered to be a major cause of death in 1,600 individuals/year [1].

Inflammatory bowel disease (IBD) is the third most significant condition that increases the overall risk of developing CRC, after familial adenomatous polyposis (FAP) and Lynch syndrome. The ulcerative colitis (UC)-associated CRC risk depends on disease duration and differs from that of the general population after 8–10 years [2]: the literature describes a risk of developing CRC of >2–5 times in IBD patients compared to the general population of the same age group [3–6]. The probability of developing CRC in UC patients is estimated to be 2% at 10 years, 8% at 20 years, and 18% at 30 years, regardless of disease extent [7]; however, more recent studies observed a lower incidence of 2.5% at 20 years and 7.6% at 30 years [8]. Disease severity also has an effect on cancer risk: uncontrolled inflammation was demonstrated to increase the cancer risk in UC patients [2, 9]. Other factors associated with a greater risk of cancer include concomitant primary sclerosing cholangitis (PSC), disease extent, family history, age, and presence of postinflammatory polyps [4, 9, 10]. In particular, PSC is strongly associated with IBD, especially with UC, with an increased risk of early CRC with a poor prognosis [11, 12].

This risk stratification for UC implicates modification of the timing of endoscopic surveillance. At present, colonoscopic surveillance is considered to be the best preventive strategy against CRC development in UC patients [2, 3, 13]. In order to reduce CRC morbidity and mortality, regular endoscopic follow-up is recommended [9]. European Crohn's and Colitis Organisation (ECCO) 2013 and British Society of Gastroenterology (BSG) 2010 guidelines recommend a first colonoscopy 8–10 years after disease onset, except in presence of proctitis or Crohn's colitis involving just one segment of the colorectum. If no dysplasia is found during the first colonoscopy, screening intervals will be determined and planned every 1–5 years, according to the risk stratification [10, 14]. The American Gastroenterology Association (2010) suggests beginning the surveillance 8 years after the onset of the disease with a follow-up scheduled every 1–3 years [15].

In UC-PSC patients, the greater risk justifies the necessity for endoscopic surveillance, with a yearly colonoscopy starting at PSC diagnosis [10, 16]. Ananthakrishnan et al. [17], in a retrospective study involving 6,823 IBD patients, found that having had a colonoscopy in the past 3 years reduced the CRC incidence rate from 2.7 to 1.6%; furthermore, a reduced rate of mortality was found among those patients diagnosed with CRC who had had a colonoscopy in the last 6–36 months before

diagnosis [17]. In our study, we hypothesize that CRC screening in patients with long-standing UC might be inefficient because of limited adherence to international recommendations. The main aim of this study was therefore to assess whether CRC screening of patients with long-standing UC was widely performed in clinical practice and to describe when and how it was performed. We also analyzed the technical characteristics used for the endoscopy together with the endoscopic and pathologic findings.

Methods

Study Design

We conducted a retrospective study among adult patients enrolled in the Swiss IBD Cohort Study (SIBDCS) [18]. The SIBDCS is a Swiss National Science Foundation (SNSF)-supported research initiative that comprises >3,500 patients followed up since 2006. This study is conducted under the approval of the ethics committee of University of Zurich that approved the SIBDCS.

Study Population

We included all UC patients with a disease duration of at least 8 years and a documented disease extension above the rectosigmoid junction and thus considered to be at moderate-to-high risk of developing CRC. We excluded patients having concomitant sclerosing cholangitis. Other exclusion criteria were presence of stenosis and/or fistula(e) and history of CRC.

Data Extraction

The following data were extracted from the SIBDCS databases: patient characteristics (age, gender, and disease duration), prior and current medications (immunomodulators, biologics, and 5-aminosalicylates), disease extent, colonoscopic findings, and screening intervals. Endoscopic and histopathologic details were retrieved from medical records in 8 Swiss centers (5 university hospitals and 3 private practices). We only considered endoscopies conducted after the moment of diagnosis. We collected information on the indication for the procedure (CRC screening or disease control). We referred to the European guidelines (ECCO 2013) as they are the main reference in Switzerland [10]. Endoscopic quality was assessed through the collection of the following variables: cecal intubation (yes/no), ileal intubation (yes/no), withdrawal time, use of dye-based chromoendoscopy or virtual chromoendoscopy, and number of biopsies taken. Finally, we also collected findings from screening exams.

Statistical Analyses

The aforementioned characteristics are categorical data. We present them by using raw frequencies and percentages. Continuous data were summarized by their mean and their standard deviation. We analyzed the timing from diagnosis to the first screening colonoscopy through a histogram and a cumulative distribution function. Statistical analyses were performed with STATA 14 software (StataCorp, 2015, College Station, TX, USA).

Fig. 1. Time between UC diagnosis and the first screening colonoscopy. Each bar shows the number of patients (frequency) having undergone a screening colonoscopy at the specific time point. UC, ulcerative colitis.

Fig. 2. Cumulative distribution function of the time between UC diagnosis and the first screening colonoscopy. UC, ulcerative colitis.

Results

Patient Characteristics

A total of 116 patients and 309 colonoscopies were included in the study. The mean age at diagnosis was 31 years (SD 10.4), and 47% ($n = 54$) of patients were women. Disease extent was pancolitis in 65.5% of patients ($n = 76$). After 8 years of disease duration, almost all patients had received 5-ASA ($n = 108$; 93%), 69% ($n = 80$) received immunomodulators, and 37% ($n = 43$) received biologic agents. The indication for endoscopy (Table 1) was CRC surveillance in 77% of the colonoscopies ($n = 238$), of which half were conducted when the disease was in remission and 38% when it was active. Endoscopies were performed for disease control in a fifth of the cases.

Time to First Surveillance Colonoscopy

The mean time between UC diagnosis and the first screening colonoscopy performed for CRC screening or disease control was 11.5 years (SD 7.4; median 9.4 years). The time between UC diagnosis and the first screening colonoscopy was <8 years after diagnosis for 45 patients (38.8%), between 8 and 10 years for 16 patients (13.8%), and after >10 years for 55 patients (47.4%) (Fig. 1). By looking at the cumulative distribution of this time, we observed that the first screening colonoscopy was conducted in <10 years for 53% of patients ($n = 61$) (Fig. 2). We then hypothesized that left-sided colitis patients might be screened later due to less extensive disease. To address this point, we compared the screening interval between

Table 1. Characteristics of the 309 endoscopies performed in the 116 patients included in the study

	<i>n</i> (%)
Indication for colonoscopy	
CRC screening	238 (77.0)
Disease control	64 (20.7)
Unknown	7 (2.3)
Disease activity in CRC screening colonoscopies	
Remission	132 (55.5)
Active disease	92 (20.7)
Unknown	14 (5.9)
CRC, colorectal cancer.	

patients with pancolitis and those with left-sided colitis. The median interval for pancolitis was 9.3 years ($n = 76$; IQR = 6.1–14.0, range = 0.5–37.3), while it was 9.7 years for the left-sided colitis ($n = 40$; IQR = 7.1–16.1, range = 3.4–33.7). This indicates that patients with left-sided colitis are screened at similar intervals than patients with pancolitis.

Endoscopic Quality Indicators

Reviewing the 309 endoscopic reports revealed a proportion of cecal intubation of 94.5% ($n = 292$) and of ileal intubation of 84.1% ($n = 260$). Quality of bowel preparation was documented in 70.2% of the exams. When documented, bowel preparation was reported as good to

Fig. 3. Quality of bowel preparation for the 309 endoscopic procedures.

Table 2. Quality indicators of screening colonoscopies ($n = 309$)

	N (%)
Cecal intubation	292 (94.5)
Ileal intubation	260 (84.1)
Mean (SD) withdrawal time	16.4 (11.5)
Chromoendoscopy	
Yes	23 (7.4)
No	270 (87.4)
Unknown	16 (5.2)
Virtual chromoendoscopy	
Yes	48 (15.5)
No	247 (79.9)
Unknown	14 (4.5)
Mean number (SD) of biopsies taken during white-light endoscopies	19.3 (15.3)

excellent in 190 procedures and bad to moderate in 27 (Fig. 3). Withdrawal time was documented in 37 colonoscopies (12.0%) with a mean of 16.4 min (SD 11.5). Chromoendoscopy was used in 7.4% of the procedures ($n = 23$) and virtual chromoendoscopy (NBI, FICE, or iScan) in 15.5%. The mean number of biopsies taken during white-light colonoscopy was 19.3 (SD 15). The total number of dysplasia observed in random and target biopsies is 19, corresponding to 6.2% of all colonoscopies carried out (Table 2). No cancers were found.

Discussion

In this study, we were interested in exploring whether CRC surveillance was conducted in long-standing UC patients at moderate-to-severe risk and whether gastroenter-

ologists followed the guidelines in terms of time to screening endoscopy procedures. We found some differences between daily practice and the international recommendations.

Overall, surveillance colonoscopies should be conducted during a disease remission phase, as ongoing inflammation raises the risk of higher false-positive rates for dysplasia detection. Nevertheless, in patients with chronic long-standing severe UC, screening may be performed considering the risk stratification, as those patients have a high risk of developing cancer [10, 14, 19]. International guidelines (ECCO and BSG) consider the starting point of colonoscopic surveillance should be set at 8–10 years after diagnosis, given that the CRC-UC risk depends on disease duration and differs from that of the general population after this time. In our study, the explicit indication for the first screening colonoscopy was mentioned in 77.9% of the procedures. Only 52.6% of all colonoscopies were performed <10 years after diagnosis. Altogether, those data demonstrate that surveillance colonoscopy was only performed in a subset of patients. It also showed that a large number of patients had a screening colonoscopy during the active phase of the disease, which hampered the expected state-of-the-art surveillance procedures. In our study, the screening interval between patients with pancolitis (9.3 years) and those with left-sided colitis (9.7 years) was similar.

The effectiveness of colonoscopy in order to reduce CRC incidence and mortality largely depends on the quality of the endoscopic exam [20]. Some quality indicators include bowel preparation quality, withdrawal time, cecal intubation rate, endoscopist's level of expertise, and adenoma detection rate (ADR). ADR is defined as the number of colonoscopies, in which at least one polyp is found, divided by the total number of surveillance colonoscopies performed [21, 22]. The American Society for Gastrointestinal Endoscopy recommends that an overall ADR of >25% (30% for men and 20% for women) should be achieved [23].

Guidelines from the European Society of Gastrointestinal Endoscopy (ESGE) suggest that cecal and ileal intubation should occur in at least 90% of all screening colonoscopies for CRC [24]. In our population, cecal and ileal intubation was conducted in 94.5% and 84.1% of cases, respectively. Quality of bowel preparation is another important indicator of efficient endoscopic surveillance. Current guidelines recommend that *adequate* preparation should be obtained in at least 90% of all surveillance colonoscopies [24]. A retrospective study conducted on 12,787 patients showed that suboptimal bowel preparation had a significant impact on the rate of miss-

ing adenoma. There is however no clear recommendation on the correct interval to the next endoscopy after a sub-optimal bowel preparation [25]. In the present study, good-to-excellent preparation was reported in 61.5% of endoscopies, while documentation was missing for 29.8% of the procedures. Overall, these data suggest that bowel preparation should be optimized in this patient population and that endoscopic reports should be improved to better document this quality indicator.

Endoscope withdrawal time has been described as a meaningful quality indicator for surveillance colonoscopy. Guidelines (ESGE) suggest a time of at least 6 min in 90% of endoscopies [24]. In our study, the mean withdrawal time was found to be close to 16 min. However, we noticed that this parameter was very rarely documented in the reports, suggesting that few gastroenterologists are aware of the importance of this indicator. Although there was a low rate of reporting of these data, our results suggest that withdrawal time was prolonged when performing surveillance colonoscopy in a UC patient population. Putative reasons for this could be the use of chromoendoscopy or image filtering techniques such as FICE, NBI, or iScan.

Compared to a few years ago, random biopsy sampling (4 random biopsies every 10 cm) is currently debated as a first-choice strategy while targeted biopsies under chromoendoscopy arises as the gold standard. Although some studies suggest that dysplasia detection might be comparable [26], others demonstrate that random sampling is more lengthy, associated with lower diagnostic yield, and less cost-effective [27, 28].

For those reasons, European guidelines recommend the use of surface enhancement imaging strategies with targeted biopsies [29]. The surface enhancement strategy can be performed using dye-spraying methods such as indigo carmine or methylene blue or virtually via image filtering techniques. Indeed, recent data suggest that image filtering techniques are not inferior to chromoendoscopy, while the latter was associated with a longer withdrawal time [26, 28, 30]. In our study, excluding colonoscopies in which chromoendoscopy was performed, the mean number of colonic biopsies was 19.3 (SD 15.3), while this should have been of at least 40. We suppose that every center used high-definition scopes. Chromoendoscopy was performed in 23 colonoscopies (total 7.44%), and virtual chromoendoscopy was used in slightly >1/6 endoscopies. Although our study does not allow us to distinguish between chromoendoscopy underuse and inappropriate reporting, it suggests that endoscopists should pay more attention to report and use surface enhancement imaging strategies for screening colonoscopies.

On the practical side, we suggest that a standardization of colonoscopy reports would simplify the work of the operators; at the same time, improved education of patients and doctors concerning current international guidelines could increase compliance and practical outcomes. This screening strategy is suggested by international guidelines (ECCO, AGA, and BSG) and supported by the current literature; however, in our opinion, it deserves further study and investigation in order to strengthen the evidence and increase its effectiveness in clinical practice.

Despite the large body of evidence arguing for endoscopic surveillance in long-standing UC, several factors might influence patients' and doctors' adherence to these recommendations. For example, complete mucosal healing is mandatory in order to avoid bias in histological analysis and detection of dysplasia. In this regard, we mention the utility of a calprotectin test prior to screening colonoscopy to increase the likelihood to conduct the screening exam in a mucosal healing state. However, healing was not frequently obtained in the present study despite adequate medical management. In addition, as most UC patients undergo several endoscopic procedures for disease follow-up and detection of flares, they might be reluctant to undergo a colonoscopy when in remission. Few studies deal with the psychosocial impact of CRC surveillance in IBD patients, but one in particular shows that there is no impact on quality of life of patients included in a CRC surveillance program [31].

Our study has several limitations. First, this is a retrospective study with a small sample size of patients and colonoscopies with all the analyses being based on non-standardized medical charts, which may be prone to reporting bias. In addition, differences in reporting and clinical practices could technically exist between hospital and private centers. Given the limited sample size, those differences could not be addressed. Concerning the activity of the disease, we observed that a large number of endoscopies revealed active histological and endoscopic activity despite clinical remission. In addition, the timing of an endoscopic exam might influence the technical practice (chromoendoscopy having been quite recently advocated as a preferred screening method).

Conclusion

Despite current international recommendations, a significant number of UC patients did not receive an adequate endoscopic surveillance in terms of timing and

Table 3. List of parameters that should be included in a standardized endoscopy report for UC-associated colorectal cancer surveillance

Initial disease extent
Current medication
Disease activity (Mayo or UCEIS score)
Cecal intubation, yes/no
Ileal intubation, yes/no
Withdrawal time
Chromoendoscopy, yes/no
Virtual chromoendoscopy, yes/no
Type of bowel preparation
Preparation quality (Boston score)

quality. In addition, our study indicates that the quality of endoscopic exams was insufficiently documented, chromoendoscopy was seriously underused, and random biopsies were insufficient when associated with white-light endoscopy. Further studies to better understand the lack of adherence to screening recommendations and further instruction for practicing gastroenterologists should be organized to improve the endoscopic surveillance of patients with long-standing UC (Table 3).

Appendix

Members of the SIBDCS group:

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Statement of Ethics

Ethics approval was obtained from the regional Swiss Ethics Committees in which SIBDCS cohort participants were enrolled (Commission d'éthique du Canton de Vaud/Protocol No. 33/06). Written informed consent was obtained from each patient included in the study. The study was conducted in accordance with the World Medical Association Declaration of Helsinki.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Giulia Santi, Michel H Maillard, and Valérie Pittet realized the study design and the data collection from medical records in the 8 Swiss centers. Jean-Benoît Rossel and Valérie Pittet performed the

data extraction from the SIBDCS databases and performed the statistical analysis. Pierre Michetti and Florian Froehlich were involved in planning and supervising the project. All authors contributed to the writing of the manuscript.

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