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CLINICAL AT

Comparison of Targeted vs Random Biopsies for Surveillance of Ulcerative Colitis-Associated Colorectal Cancer

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This article has an accompanying continuing medical education activity, also eligible for MOC credit, on page e23. Learning Objective: Upon completion of this evaluation, successful learners will be able to manage patients with ulcerative colitis who are at high risk for the development of colorectal cancer.

See Covering the Cover synopsis on page 1043.

BACKGROUND & AIMS: A random biopsy is recommended for surveillance of ulcerative colitis (UC)-associated colorectal cancer. However, a targeted biopsy might be more effective. We conducted a randomized controlled trial to compare rates of neoplasia detection by targeted vs random biopsies in patients with UC. **METHODS:** We performed a study of 246 patients with UC for 7 years or more, seen at 52 institutions in Japan from October 1, 2008 through December 31, 2010. Patients were randomly assigned to the random group (4 random biopsies collected every 10 cm in addition to targeted biopsies, n = 122) or the target group (biopsies collected from locations of suspected neoplasia, n = 124). The primary end point was the number of neoplastic lesions detected in a single surveillance colonoscopy. We estimated the ratio and difference in the mean number of neoplastic lesions between the groups. We also evaluated the non-inferiority between the groups as an exploratory study. A non-inferiority margin of 0.65 (0.13 of 0.20) was considered for the ratio of the mean number of neoplastic lesions between groups. **RESULTS:** The mean number of biopsies found to contain neoplastic tissue per colonoscopy was 0.211 (24 of 114) in the target group and 0.168 (18 of 107) in the random group (ratio of 1.251; 95% confidence interval, 0.679–2.306). The lower limit was above the non-inferiority margin of 0.65. Neoplasias were detected in 11.4% of patients in the target group and 9.3% of patients in

the random group ($P = .617$). Larger numbers of biopsy samples per colonoscopy were collected in the random group (34.8 vs 3.1 in the target group; $P < .001$), and the total examination time was longer (41.7 vs 26.6 minutes in the target group; $P < .001$). In the random group, all neoplastic tissues found in random biopsies were collected from areas of the mucosa with a history or presence of inflammation. **CONCLUSIONS:** In a randomized controlled trial, we found that targeted and random biopsies detect similar proportions of neoplasias. However, a targeted biopsy appears to be a more cost-effective method. Random biopsies from areas without any signs of present or past inflammation were not found to contain neoplastic tissues. Clinical Trial Registry: UMIN000001608.

Keywords: Dysplasia; Random Biopsy; Colonoscopy; IBD.

In long-standing ulcerative colitis (UC), the risk for colorectal cancer (CRC) increases as disease duration increases. The cumulative risk reaches 7.5%−18.4% at 30 years after onset of the disease.[1–3] We previously showed that at an advanced stage, UC-associated CRC has poorer survival rates than sporadic CRC.[4] Therefore, early detection of UC-associated CRC is essential for successful management of long-standing UC. However, it is not always easy to endoscopically identify UC-associated CRC or dysplasia, as these lesions can be either invisible or very difficult to identify.[5] Therefore, the guidelines recommend use of non-targeted biopsy (random biopsy) for surveillance colonoscopy, in which either 4 biopsy specimens for every 10 cm or ≥33 biopsy specimens are obtained.[6–9] However, random biopsy has been recognized to be costly and time-consuming[10] and targeted biopsy has recently received much attention as an alternative.[11–13] Studies have found that 61%−84% of neoplastic lesions could be visualized by recent endoscopy[14–16] and, therefore, the guidelines suggest the possible use of targeted biopsy in place of random biopsy to improve the efficacy of surveillance.[17,18] In targeted biopsy, specimens are obtained only when endoscopic findings indicate the possibility of neoplasia, leading to a smaller number of samples and resulting in a more cost-effective method. However, very few studies have so far directly and prospectively compared the efficacy of targeted biopsy with that of random biopsy, and it still remains controversial as to whether targeted biopsy should completely replace random biopsy. Therefore, the Research Group for Intractable Inflammatory Bowel Disease of the Ministry of Health, Labour and Welfare of Japan and the Japanese Society for Cancer of the Colon and Rectum (JSCCR) conducted a randomized controlled trial to compare the 2 different biopsy methods. The aim of the present study was to evaluate whether targeted biopsy would show the comparable neoplasia detection rates with a random biopsy.

Methods

Study Design and Oversight

This trial was designed as an exploratory multicenter randomized controlled trial to provide an estimate of the mean number of neoplastic biopsy samples per colonoscopy for a targeted biopsy and a random biopsy in cancer surveillance for long-standing UC patients (Figure 1). The non-inferiority was additionally evaluated with a non-inferiority margin of 0.65 for the ratio of mean number of neoplastic lesions identified between groups. The protocol was set up by the Research Group for Intractable Inflammatory Bowel Disease of the Ministry of Health, Labour and Welfare of Japan and JSCCR. This study was approved by the ethics committee of JSCCR and the Institutional Review Boards of all participating institutions and was conducted in accordance with the Declaration of Helsinki. All participants gave their written informed consent for study participation. An independent data and safety monitoring committee assessed the study data. All serious adverse events were reported to an independent data and safety monitoring committee. The trial is registered at the UMIN Clinical Trial Registry as UMIN000001608 (http://www.umin.ac.jp/ctr/index-j.htm) and the study protocol has been described previously.[19]

Sites and Patients

All of the participating sites (52 Japanese institutions) were members of the Research Group for Intractable Inflammatory Bowel Disease of the Ministry of Health, Labour and Welfare of Japan or JSCCR. We recruited UC patients (left-sided colitis and pancolitis) for whom 7 years or more had passed since onset of the disease. Inclusion and the exclusion criteria are shown in Supplementary Table 1.[20,21]

Study Interventions

We randomly assigned the patients to the targeted biopsy group (target group) or the step biopsy group (random group) after confirming the inclusion and exclusion criteria with the Data Center, Department of Preventive Medicine and Public Health, Keio University. Using stratified allocation, the Data Center defines the facilities and the severity of UC as stratification factors to randomly assign the patients into the target group or the random group. Unique random sequence, which had been generated by the Data Center, was sequentially applied to each patient allocation. The detailed procedures of randomization were not disclosed to researchers at the participating sites. The results of the assignment were not blinded to researchers. In the target group, specimens were obtained by a targeted biopsy. In addition, at least 1 biopsy sample was obtained in the lower rectum, even when no findings suggesting the presence of neoplasia existed. In the random group, 4 random biopsies were obtained every 10 cm. In addition, a targeted biopsy was performed in regions suspected of neoplasia. Panchromoendoscopy was not performed routinely because the study was concluded before the SCENIC (Surveillance for Colorectal Endoscopic Neoplasia Detection

Abbreviations used in this paper: CRC, colorectal cancer; JSCCR, Japanese Society for Cancer of the Colon and Rectum; UC, ulcerative colitis.

Most current article

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